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As submitted confidentially with the Securities and Exchange Commission on May 13, 2016. This draft registration statement has not been publicly filed with the Securities and Exchange Commission and all information herein remains strictly confidential.

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-1
REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

CRISPR THERAPEUTICS AG

(Exact name of Registrant as specified in its Charter)

Switzerland	2836	Not Applicable
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

CRISPR Therapeutics AG
Aeschenvorstadt 36
4051 Basel
Switzerland
+41 61 228 7800
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Dr. Rodger Novak
Chief Executive Officer
CRISPR Therapeutics, Inc.
200 Sidney St.
Cambridge, Massachusetts 02139
(617) 315-4600
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Mitchell S. Bloom	**Patrick O'Brien**
Robert E. Puopolo	**Paul Kinsella**
Goodwin Procter LLP	**Ropes & Gray LLP**
Exchange Place	**Prudential Tower**
53 State Street	**800 Boylston Street**
Boston, MA 02109	**Boston, MA 02199**
(617) 570-1000	**(617) 951-7000**

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒ (Do not check if a smaller reporting company)	Smaller reporting company	☐

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Proposed maximum aggregate offering price(1)(2)	Amount of registration fee(3)
Common shares, nominal value CHF 0.10 per share	$	$

(1) Estimated solely for the purpose of computing the amount of the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.
(2) Includes offering price of shares that the underwriters have the option to purchase to cover over-allotments, if any.
(3) Calculated pursuant to Rule 457(o) under the Securities Act of 1933, as amended, based on an estimate of the proposed maximum aggregate offering price.

The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Commission, acting pursuant to such Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION DATED MAY 13, 2016

PRELIMINARY PROSPECTUS

Shares

CRISPR Therapeutics AG

Common Shares

$ per share

This is the initial public offering of our common shares. We are selling common shares. We currently expect the initial public offering price to be between $ and $ per common share.

We have granted the underwriters an option to purchase up to additional common shares to cover over-allotments.

We intend to apply to have our common shares listed on the NASDAQ Global Market under the symbol "CRSP."

We are an "emerging growth company" as defined under the federal securities laws and, as such, will be subject to reduced public company reporting requirements. See "Prospectus Summary—Implications of Being an Emerging Growth Company."

Investing in our common shares involves risks. See "Risk Factors" beginning on page 11.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public Offering Price	$	$
Underwriting Discounts(1)	$	$
Proceeds to CRISPR Therapeutics AG (before expenses)	$	$

(1) See "Underwriting" beginning on page 190 for additional information regarding total underwriter compensation.

Bayer Global Investments B.V., an existing shareholder and an affiliate of Bayer HealthCare LLC, our joint venture partner, has agreed to purchase from us concurrently with this offering in a private placement up to $35 million of our common shares at a price per share equal to the initial public offering price. See "Concurrent Private Placement."

The underwriters expect to deliver the shares to purchasers on or about , 2016 through the book-entry facilities of The Depository Trust Company.

Citigroup **Piper Jaffray** **Barclays**

Guggenheim Securities

, 2016.

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We are organized under the laws of Switzerland and our registered office and domicile is located in Basel, Switzerland. Moreover, certain of our directors and executive officers are not residents of the United States, and all or a substantial portion of the assets of such persons are located outside the United States. As a result, it may not be possible for investors to effect service of process within the United States upon us or upon such persons or to enforce against them judgments obtained in U.S. courts, including judgments in actions predicated upon the civil liability provisions of the federal securities laws of the United States. We have been advised by our Swiss counsel that there is doubt as to the enforceability in Switzerland of original actions, or of actions for enforcement of judgments of U.S. courts of civil liabilities to the extent solely predicated upon the federal and state securities laws of the United States. See "Enforcement of Judgments" for additional information.

Unless otherwise indicated or the context otherwise requires, all references in this prospectus to "CRISPR," the "Company," "we," "our," "ours," "us" or similar terms refer to CRISPR Therapeutics AG and its consolidated subsidiaries.

We own various trademark and unregistered trademarks, including CRISPR and our corporate logo. All other trade names, trademarks and service marks of other companies appearing in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their

respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend to use or display other companies' trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Our consolidated financial statements are presented in U.S. dollars in accordance with U.S. generally accepted accounting principles. In addition, we prepare statutory accounts in Swiss Francs in accordance with Swiss statutory law. The Swiss statutory accounting principles may materially differ from U.S. generally accepted accounting principles. The terms "dollar," "USD" or "$" refer to U.S. dollars and the term "Swiss Franc" and "CHF" refer to the legal currency of Switzerland, unless otherwise indicated.

You should rely only on the information contained in this prospectus or in any free writing prospectus prepared by us or on our behalf. We and the underwriters have not authorized anyone to provide any information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we may have referred you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you.

Neither we nor the underwriters are making an offer to sell the common shares in any jurisdiction where the offer or sale is not permitted. This offering is being made in the United States and elsewhere solely on the basis of the information contained in this prospectus. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or any sale of the common shares. Our business, financial condition, results of operations and prospects may have changed since the date on the front cover of this prospectus. Information contained on our website is not a part of this prospectus. You are required to inform yourselves about, and to observe any restrictions relating to, this offering and the distribution of this prospectus outside of the United States.

SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary may not contain all the information that may be important to you, and we urge you to read this entire prospectus carefully, including the "Risk Factors," "Business" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections and our consolidated financial statements, including the notes thereto, included elsewhere in this prospectus, before deciding to invest in our common shares.

Our Business

Overview

We are a leading gene editing company focused on the development of CRISPR/Cas9-based therapeutics. CRISPR/Cas9 is a revolutionary gene editing technology that allows for precise, directed changes to genomic DNA. The application of CRISPR/Cas9 for gene editing was co-invented by one of our scientific founders, Dr. Emmanuelle Charpentier who, along with her collaborators, published work elucidating how CRISPR/Cas9, a naturally occurring viral defense mechanism found in bacteria, can be adapted for use in gene editing. We are applying this technology to treat a broad set of rare and common diseases by disrupting, correcting or regulating the disease related genes. We believe that our scientific expertise, together with our approach, may enable an entirely new class of highly active and potentially curative treatments for patients for whom current biopharmaceutical approaches have had limited success.

We are pursuing a two-pronged product development strategy using both *ex vivo* and *in vivo* approaches. Our most advanced programs in hemoglobinopathies use an *ex vivo* approach, whereby cells are harvested from a patient, treated with a CRISPR/Cas9-based therapeutic and reintroduced into the patient. Beyond these lead programs, we are pursuing a number of additional *ex vivo* applications, as well as select *in vivo* applications whereby the CRISPR/Cas9 therapeutic is delivered directly to target cells within the human body. Our initial *in vivo* applications will leverage well-established delivery technologies for gene-based therapeutics.

Given the numerous potential therapeutic applications for CRISPR/Cas9, we have partnered strategically to broaden the indications we can pursue and accelerate development of programs by accessing specific disease-area expertise. We have established collaborations with Bayer AG and its subsidiaries, or Bayer, and Vertex Pharmaceuticals, Incorporated, or Vertex, which will provide over $400 million, inclusive of estimated spending on funded programs, as well as access to distinctive capabilities. We have assembled a team with extensive experience in drug discovery and clinical development to successfully bring CRISPR/Cas9-based therapeutics to patients. We believe our highly experienced team, differentiated product development strategy, partnerships and intellectual property position us as a leader in the development of CRISPR/Cas9-based therapeutics.

Our Strategy

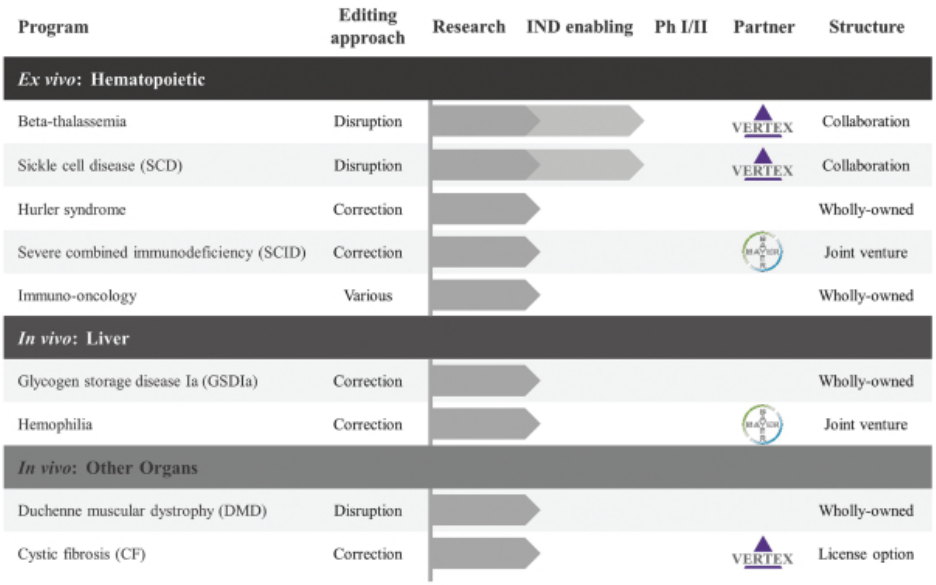
Our mission is to create transformative gene-based medicines for serious human diseases. Key components of our strategy to enable us to achieve this mission include:

- *Focus on the Hematopoietic System Through* Ex Vivo *Approaches.*
  - — Rapidly Advance Our Two Lead Programs in Hemoglobinopathies, Sickle Cell Disease and Beta-Thalassemia.
  - — Apply our Hematopoietic Gene Editing Capabilities in Other Indications.

- *Pursue Select Indications Requiring* In Vivo *Approaches.*
  - — Target the Liver Using Readily Available Delivery Technologies.
  - — Optimize Delivery Technologies to Target Select *In Vivo* Indications Outside the Liver.
- *Continue to Foster and Strategically Leverage Our Collaborations with Bayer and Vertex.*
- *Advance our Leading Position in the Field of Gene Editing.*

Our Pipeline

We have established a portfolio of programs by selecting disease targets based on a number of criteria, including high unmet medical need, advantages of CRISPR/Cas9 relative to alternative approaches, technical feasibility and the time required to advance the product candidate into and through clinical trials. We have initiated programs in three primary areas: (i) *ex vivo* programs involving gene editing of hematopoietic cells,
(ii) *in vivo* programs targeting the liver and (iii) additional *in vivo* programs targeting other organ systems, such as muscle and lung. The following table summarizes the current status of our product development pipeline:



Ex Vivo *Hematopoietic Programs.*

We are primarily utilizing *ex vivo* approaches to treat diseases related to the hematopoietic system, which is the system of organs and tissues, such as bone marrow, the spleen and lymph nodes, involved in the production of blood. When a suitable donor can be found, many of the hematopoietic system diseases we are targeting are treated with allogeneic hematopoietic stem cell transplants, or allo-HSCT. Patients who undergo allo- HSCT face a high risk of complications such as infections related to immunosuppression, transplant rejection and graft-versus-host disease.

Our Lead Programs—Hemoglobinopathies

Our lead programs aim to develop a single, potentially transformative CRISPR/Cas9-based therapy to treat both beta-thalassemia and sickle cell disease, or SCD. These diseases are caused by specific mutations of the beta globin gene. A number of factors make these attractive lead indications, including: (i) high unmet medical need, (ii) compelling market potential, (iii) well understood genetics and (iv) the ability to employ an *ex vivo* gene disruption strategy.

Beta-thalassemia is caused by mutations that give rise to insufficient expression of the beta globin protein, resulting in anemia requiring regular blood transfusions. SCD is an inherited disorder caused by a mutation in the beta globin gene resulting in abnormal red blood cells, which obstruct blood vessels, resulting in a variety of severe symptoms and early mortality. The total worldwide annual incidence of beta-thalassemia and SCD is estimated to be 60,000 and 300,000 births, respectively.

Our therapeutic approach to treating these diseases employs gene editing to upregulate the expression of the gamma globin protein, a hemoglobin subunit that is commonly present only in newborn infants. Hemoglobinopathy patients who maintain high levels of gamma globin throughout their life are asymptomatic or have mild diseases. We believe our *ex vivo* gene editing approach, utilizing the patient's own cells, will provide better safety and efficacy than all currently available treatments.

Other Hematopoietic Programs

That there are numerous diseases that are potentially treatable through *ex vivo* gene editing of the hematopoietic system. We plan to apply the capabilities we are developing in hemoglobinopathies to treat other diseases. We have launched programs in two such diseases, severe combined immunodeficiency disease, or SCID, and Hurler syndrome, a genetic metabolic disorder. In addition, we are utilizing our *ex vivo* gene editing expertise to advance our efforts in cell therapies for immuno-oncology applications.

In Vivo *Programs*

We are pursuing a number of *in vivo* indications in parallel with our *ex vivo* programs, which will involve delivery of CRISPR/Cas9 therapeutics directly to target tissues within the human body. Our initial *in vivo* applications will target the liver, leveraging well-established delivery technologies. We intend to customize and use these delivery technologies for programs in hemophilia and genetic diseases of liver metabolism, including Glycogen Storage Disease Ia, or GSDIa.

We intend to optimize delivery technologies to target select *in vivo* indications outside the liver such as Duchenne muscular dystrophy and cystic fibrosis. We believe that our CRISPR/Cas9 gene editing technology is well suited to address these diseases, both of which have significant patient populations with high unmet medical need. We are working internally, as well as through third-party collaborations, to optimize viral and non-viral delivery technologies for use in these diseases.

Further Unlocking the Potential of Our CRISPR/Cas9 Platform

We are also working to optimize our CRISPR/Cas9 platform. Our key areas of focus are:

- *Optimizing the Cas9 Protein*: Reduce the size and potential immunogenicity of the Cas9 protein while improving specificity and efficiency.
- *Guide RNA Selection*: Combine bioinformatics and experimental assays to identify guide RNAs with high efficiency and no off-target cutting.

- *Delivery of CRISPR/Cas9 to Target Cells*: Develop next-generation delivery technologies to access additional organ systems.
- *Efficiency of Correction*: Achieve high efficiency of correction across all cell types and enable new therapeutic strategies.
- *Cellular Engineering*: Improve the *ex vivo* cell collection, manipulation and administration process for a variety of stem cell types.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the "Risk Factors" section of this prospectus immediately following this prospectus summary. These risks include the following:

- *We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future and we have never generated revenue from product sales and may never be profitable.*
- *We are very early in our development efforts. All of our product candidates are still in preclinical development and it will be many years before we or our collaborators commercialize a product, if ever.*
- *Our CRISPR/Cas9 gene editing product candidates are based on a new gene editing technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval, if at all. There have only been a limited number of clinical trials of product candidates based on gene editing technology and no gene editing products have been approved in the United States or in the European Union.*
- *The FDA, the NIH and the EMA have demonstrated caution in their regulation of gene therapy treatments, and ethical and legal concerns about gene therapy and genetic testing may result in additional regulations or restrictions on the development and commercialization of our product candidates, which may be difficult to predict.*
- *Positive results from early preclinical studies of our product candidates are not necessarily predictive of the results of later preclinical studies and any future clinical trials of our product candidates. If we cannot replicate the positive results from our earlier preclinical studies of our product candidates in our later preclinical studies and future clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.*
- *Gene editing products are novel and may be complex and difficult to manufacture. We could experience manufacturing problems that result in delays in the development or commercialization of our product candidates or otherwise harm our business.*
- *Adverse public perception of gene editing and cellular therapy products may negatively impact demand for, or regulatory approval of, our product candidates.*
- *The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors and others in the medical community.*
- *We face significant competition in an environment of rapid technological change and the possibility that our competitors may achieve regulatory approval before us or develop therapies that are more advanced or effective than ours, which may harm our business and financial condition, and our ability to successfully market or commercialize our product candidates.*

- *Our collaborators and strategic partners may control aspects of our clinical trials, which could result in delays and other obstacles in the commercialization of our proposed products and materially harm our results of operations.*
- *If we are unable to adequately protect our proprietary technology or obtain and maintain patent protection for the products we develop and for our technology and product candidates, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize any product candidates we may develop, and our technology may be adversely affected.*
- *Some of our in-licensed patent applications are subject to priority disputes and Inventorship disputes, including an active interference proceeding with the Broad Institute and Massachusetts Institute of Technology, in front of the United States Patent and Trademark Office. In addition, our owned and in-licensed patents and other intellectual property may be subject to further priority disputes or to inventorship disputes and similar proceedings. If we or our licensors are unsuccessful in any of these proceedings, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms or at all, or to cease the development, manufacture, and commercialization of one or more of the product candidates we may develop, which could have a material adverse impact on our business.*
- *The intellectual property landscape around gene editing technology, including CRISPR/Cas9, is highly dynamic, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.*
- *Our status as a Swiss corporation means that our shareholders enjoy certain rights that may limit our flexibility to raise capital, issue dividends and otherwise manage ongoing capital needs.*

Concurrent Private Placement

Bayer Global Investments B.V., an existing shareholder and an affiliate of Bayer HealthCare LLC, our joint venture partner, has agreed to purchase from us concurrently with this offering in a private placement up to $35 million of our common shares at a price per share equal to the initial public offering price. See “Concurrent Private Placement.”

Corporate Information

We were incorporated as a Swiss stock corporation *(Aktiengesellschaft)* on October 31, 2013 under the name Inception Genomics AG. We changed our name to CRISPR Therapeutics AG on April 28, 2014. Our principal executive offices are located at Aeschenvorstadt 36, 4051 Basel, Switzerland and our telephone number is + 41 61 228 7800. Our website is www.crisprtx.com. Our website and the information contained therein or connected thereto are not incorporated into this prospectus or the registration statement of which it forms a part.

Implications of Being an Emerging Growth Company

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced reporting and other burdens that are otherwise applicable generally to public companies. These provisions include:

- a requirement to have only two years of audited financial statements in addition to any required interim financial statements and correspondingly reduced disclosure in the Management's Discussion and Analysis of Financial Condition and Results of Operations disclosure in the registration statement of which this prospectus forms a part;
- reduced disclosure about our executive compensation arrangements; and
- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to the Section 404 of the Sarbanes-Oxley Act of 2002.

We may take advantage of these provisions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company upon the earliest to occur of (i) the last day of the fiscal year in which we have more than $1.0 billion in annual revenue; (ii) the date we qualify as a "large accelerated filer," with at least $700 million of equity securities held by non-affiliates; (iii) the issuance, in any three-year period, by our Company of more than $1.0 billion in non-convertible debt securities; and (iv) the last day of the fiscal year ending after the fifth anniversary of this offering. We may choose to take advantage of some but not all of these reduced burdens. For example, Section 107 of the JOBS Act provides that an emerging growth company can use the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. However, we have irrevocably elected not to avail ourselves of the extended transition period for complying with new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

THE OFFERING

Common shares offered by us	shares
Concurrent Private Placement	Bayer Global Investments B.V., or Bayer BV, has agreed to purchase from us concurrently with this offering in a private placement up to $35 million of our common shares at a price per share equal to the initial public offering price, or shares, assuming an initial public offering price of $ per common share, which is the midpoint of the price range set forth on the cover page of this prospectus. We will receive the full proceeds from the sale and will not pay any underwriting discounts or commissions with respect to the common shares that are sold in the private placement. The sale of these common shares to Bayer BV will not be registered under the Securities Act of 1933, as amended, and these common shares will be subject to a 180-day lock-up agreement with the underwriters in this offering. We refer to the private placement of these common shares as the concurrent private placement.
Common shares to be outstanding immediately after this offering and the concurrent private placement	shares
Over-allotment option	shares
Use of proceeds	We estimate that the net proceeds to us from this offering, excluding the proceeds from the concurrent private placement, will be approximately $ million, or approximately $ million if the underwriters exercise their over-allotment option to purchase additional common shares in full, assuming an initial public offering price of $ per common share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Our proceeds from the sale of common shares in the concurrent private placement will be approximately $ million. We intend to use the net proceeds from this offering and the concurrent private placement to advance the development of our hemoglobinopathy programs, progress additional pipeline candidates, further optimize our CRISPR/Cas9 platform and for manufacturing, working capital and general corporate purposes. See “Use of Proceeds” for a more complete description of the intended use of proceeds from this offering and the concurrent private placement.
Risk factors	See “Risk Factors” and the other information included in this prospectus for a discussion of factors you should consider before deciding to invest in our common shares.
Proposed NASDAQ Global Market symbol	“CRSP”

The number of our common shares to be outstanding after this offering and the concurrent private placement is based on 7,309,533 common shares outstanding as of December 31, 2015, but excludes:

- 581,999 of our common shares issuable upon the exercise of options outstanding under our 2015 Stock Option and Grant Plan, or the 2015 Stock Option Plan, as of December 31, 2015 at a weighted-average exercise price of $10.44 per common share;
- the conversion of the convertible loan, including accrued interest, issued in October 2015 into 1,233,296 Series B Preferred Shares;
- 42,838 unvested restricted share awards granted under our 2015 Stock Option Plan;
- the issuance of 98,405 common shares to Dr. Emmanuelle Charpentier immediately prior to the closing of this offering pursuant to a call option agreement, dated March 20, 2015, between us and Dr. Emmanuelle Charpentier, or the Call Option Agreement;
- of our common shares reserved for future issuance under our 2016 Stock Option and Incentive Plan, or the 2016 Stock Option Plan, which will become effective immediately prior to the completion of this offering; and
- common shares reserved for issuance under our 2016 Employee Stock Purchase Plan, or ESPP, which will become effective immediately prior to the completion of this offering.

Unless otherwise indicated, all information contained in this prospectus reflects the completion of a -for-one share split and assumes:

- no issuance of any common shares reserved for future issuance under our 2016 Stock Option Plan or exercise of the options outstanding under our 2015 Stock Option Plan;
- the conversion of all 5,651,105 of our outstanding preferred shares into common shares on a one-for-one basis immediately prior to the closing of this offering;
- the filing and effectiveness of our amended articles of association and creation of authorized and conditional share capital of common shares upon closing of this offering;
- the issuance and sale by us in the concurrent private placement of common shares to Bayer BV, assuming an initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus; and
- no exercise of the underwriters' over-allotment option to purchase up to additional common shares.

SUMMARY CONSOLIDATED FINANCIAL DATA

The following summary consolidated historical financial data should be read in conjunction with "Selected Consolidated Financial Data," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements, including the notes thereto, included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future and results of interim periods are not necessarily indicative of results for the entire year.

The summary consolidated income statement data and consolidated balance sheet data for and as of the years ended December 31, 2015 and 2014 are derived from our audited consolidated financial statements included elsewhere in this prospectus.

We maintain our books and records in, and our audited consolidated financial statements are prepared and presented in accordance with, U.S. generally accepted accounting principles.

	Year Ended December 31,	
	2014	2015
	(in thousands, except share and per share amounts)	
Statement of Operations Data:		
Collaboration revenue	$ —	$ 247
Operating expenses:		
Research and development	1,513	12,573
General and administrative	5,114	13,403
Total operating expenses	6,627	25,976
Operating loss	(6,627)	(25,729)
Other expense, net	(236)	(92)
Benefit from (provision for) income taxes	63	(7)
Net loss	(6,800)	(25,828)
Foreign currency translation adjustment	(2)	(6)
Comprehensive loss	$ (6,802)	$ (25,834)
Reconciliation of net loss to net loss attributable to common shareholders:		
Net loss	(6,800)	(25,828)
Loss attributable to noncontrolling interest	536	325
Loss on extinguishment of redeemable convertible preferred shares	(745)	—
Net loss attributable to common shareholders	$ (7,009)	$ (25,503)
Net loss per share attributable to common shareholders, basic and diluted	$ (6.56)	$ (16.88)
Weighted-average common shares outstanding, basic and diluted(1)	1,068,000	1,511,225
Pro-forma net loss per share, basic and diluted (unaudited)		(4.20)
Pro-forma weighted-average common shares outstanding, basic and diluted (unaudited)		6,072,412

(1) See Note 2 in the notes to our consolidated financial statements appearing at the end of this prospectus for a description of the method used to calculate basic and diluted net loss per share and pro forma basic and diluted net loss per share.

The table below presents our balance sheet data at December 31, 2015:

- on an actual basis;
- on a pro forma basis to give effect to:
  - (i) the conversion of all 5,651,105 of our outstanding preferred shares into common shares on a one-for-one basis immediately prior to the closing of this offering;
  - (ii) the issuance of 98,405 common shares to Dr. Emmanuelle Charpentier immediately prior to the closing of this offering pursuant to the Call Option Agreement;
  - (iii) the conversion of the convertible loan, including accrued interest, issued in October 2015 into 1,233,296 Series B Preferred Shares, and then into common shares on a one-for-one basis immediately prior to the closing of this offering; and
  - (iv) the filing and effectiveness of our amended and restated articles of association and creation of authorized share capital of common shares upon closing of this offering.
- on a pro forma as adjusted basis to further reflect:
  - (i) the receipt of the estimated net proceeds from the sale of common shares in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the underwriting discount and estimated expenses payable by us; and
  - (ii) the issuance and sale by us in the concurrent private placement of common shares to Bayer BV, assuming an initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus.

	As of December 31, 2015		
	Actual	Pro Forma	Pro Forma As Adjusted(1)
		(in thousands)	
Balance Sheet Data:			
Cash and cash equivalents	$155,961	$155,961	$ —
Working capital	146,685	146,685	—
Total assets	159,423	159,423	—
Redeemable convertible preferred shares	64,521	—	—
Total shareholders' (deficit) equity	$ (29,124)	$ 73,733	$ —

(1) A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) each of the pro forma as adjusted additional paid in capital and total shareholders' equity by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the underwriting discount and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase (decrease) of 1,000,000 in the number of shares offered by us would increase (decrease) pro forma additional paid in capital and total shareholders' equity and capitalization by $ million, assuming an initial public offering price of $ per share, after deducting the underwriting discount and estimated offering expenses payable by us.

RISK FACTORS

Investing in our common shares involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this prospectus and any related free writing prospectus, including our consolidated financial statements and the related notes thereto and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common shares. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common shares could decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations

Risks Related to Our Financial Position and Need for Additional Capital

We Have Incurred Significant Operating Losses Since Our Inception And Anticipate That We Will Incur Continued Losses For The Foreseeable Future.

We have funded our operations to date through proceeds from sales of preferred shares, convertible securities and payments received in connection with our joint venture with Bayer HealthCare LLC, or Bayer Healthcare, and collaboration agreement with Vertex Pharmaceuticals, Incorporated, or Vertex. Since inception, we have incurred significant operating losses. Our net loss was $6.8 million and $25.8 million for the years ended December 31, 2014 and 2015, respectively. As of December 31, 2015, we had an accumulated deficit of $33.9 million. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our shareholders' deficit and working capital. We anticipate that our expenses will increase substantially if and as we:

- continue our current research programs and our preclinical development of product candidates from our current research programs;
- seek to identify additional research programs and additional product candidates;
- initiate preclinical studies and clinical trials for any product candidates we identify and choose to develop;
- maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals for any of our product candidates that successfully complete clinical trials;
- further develop our gene editing technology;
- hire additional clinical, quality control and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product candidate development;
- acquire or in-license other technologies;
- ultimately establish a sales, marketing, and distribution infrastructure to commercialize any products for which we may obtain marketing approval; and
- operate as a public company.

As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing gene editing product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

We Have Never Generated Revenue From Product Sales And May Never Be Profitable.

To date, we have not generated any revenue from our programs and product candidates and do not expect to generate any revenue from the sale of our product candidates in the near future, if ever. We will not generate significant product revenue unless and until we, or our partners, obtain marketing approval of, and begin to sell one or more of our product candidates. Our ability to generate product revenue depends on a number of factors, including, but not limited to:

- identifying product candidates and completing research and preclinical and clinical development of any product candidates we may identify;
- seeking and obtaining regulatory and marketing approvals for any of our product candidates for which we complete clinical trials;
- launching and commercializing any of our product candidates for which we obtain regulatory approval by establishing a sales force, marketing and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- qualifying for adequate coverage and reimbursement by government and third-party payors for any of our product candidates for which we obtain regulatory and marketing approval;
- developing, maintaining and enhancing a sustainable, scalable, reproducible, and transferable manufacturing process for the product candidates we may develop;
- establishing and maintaining supply chain and manufacturing relationships with third parties that can provide adequate products and services, in both amount and quality, to support clinical development and the market demand for any of our product candidates for which we obtain regulatory and marketing approval;
- obtaining market acceptance of any product candidates we may develop as viable treatment options;
- addressing competing technological and market developments;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter and performing our obligations in such collaborations;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how;
- avoiding and defending against third-party interference or infringement claims;
- attracting, hiring, and retaining qualified personnel; and
- implementing internal systems and infrastructure, as needed.

Even if one or more of the product candidates we may develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or the EMA, or other regulatory authorities to perform clinical and other studies in addition to those that we anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our Company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our Company also could cause you to lose all or part of your investment.

Even If We Consummate This Offering And The Concurrent Private Placement With Bayer Global Investments B.V., or Bayer BV, We Will Need To Raise Substantial Additional Funding, Which Will Dilute Our Shareholders. If We Are Unable To Raise Capital When Needed, We Would Be Forced To Delay, Reduce Or Eliminate Some Of Our Product Development Programs Or Commercialization Efforts.

The development of gene editing product candidates is capital intensive. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate preclinical studies and clinical trials for and seek marketing approval for our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of Bayer BV or Vertex, or other future collaborators. We may also need to raise additional funds sooner if we choose to pursue additional indications or geographies for our product candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate certain of our research and development programs or future commercialization efforts.

As of December 31, 2015, we had cash of approximately $156 million. We expect that the net proceeds from this offering and the concurrent private placement, together with our existing cash and cash equivalents, and anticipated research support under our joint venture with Bayer BV and collaboration agreement with Vertex, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 24 months.

Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of establishing and maintaining a supply chain for the development and manufacture of our product candidates;
- the success of our current collaborations;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we obtain;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of establishing or contracting for manufacturing capabilities if we obtain regulatory approvals to manufacture our product candidates;
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market our product candidates; and
- our ability to establish and maintain healthcare coverage and adequate reimbursement.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our shareholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our shareholders and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

We Have A Very Limited Operating History, Which May Make It Difficult To Evaluate Our Technology And Product Development Capabilities And Predict Our Future Performance.

We are very early in our development efforts and all of our lead programs are still in the discovery stage. We were formed in October 2013, have no products approved for commercial sale and have not generated any revenue from product sales. Our ability to generate product revenue or profits, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. We may never be able to develop or commercialize a marketable product.

Each of our programs will require additional discovery research and then preclinical and clinical development, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. In addition, our product candidates must be approved for marketing by the FDA or certain other foreign regulatory agencies, including the EMA, before we may commercialize any product.

Our limited operating history, particularly in light of the rapidly evolving gene editing field, may make it difficult to evaluate our technology and industry and predict our future performance. Our very short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by very early stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

Our Ability To Use Tax Loss Carryforwards In Switzerland May Be Limited.

As of December 31, 2015, we reported tax loss carry forwards from inception through 2015 for purposes of Swiss federal direct taxes in the aggregate amount of CHF 22.0 million. Due to the expected mixed company status (in case the advance tax ruling with respect to the mixed company status will be accepted) the tax losses at cantonal level amount to CHF 4.1 million. These tax losses could be available to offset future taxable income. If not used, these tax losses will expire seven years after the year in which they were incurred. Due to our limited income, there is a high risk that the tax loss carry forwards will expire partly or entirely.

Risks Related to Our Business, Technology and Industry

We Are Very Early In Our Development Efforts. All Of Our Product Candidates Are Still In Preclinical Development And It Will Be Many Years Before We Or Our Collaborators Commercialize A Product Candidate, If Ever. If We Are Unable To Advance Our Product Candidates To Clinical Development, Obtain Regulatory Approval And Ultimately Commercialize Our Product Candidates, Or Experience Significant Delays In Doing So, Our Business Will Be Materially Harmed.

We are very early in our development efforts and have focused our research and development efforts to date on our Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) Associated protein-9 nuclease, or CRISPR/Cas9, gene editing technology, identifying our initial targeted disease indications and our initial product candidates. Our future success depends heavily on the successful development of our CRISPR/Cas9 gene editing product candidates. Currently, all of our product candidates are in preclinical development. We have also only recently begun development activities for a product candidate for the treatment of beta-thalassemia and sickle cell disease in connection with our collaboration with Vertex and have not yet identified a lead product candidate. We have invested substantially all of our efforts and financial resources in the identification and preclinical development of our current product candidates. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. For example, our research programs, including those subject to our joint venture with Bayer Healthcare and collaboration agreement with Vertex, may fail to identify potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates, or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products impractical to manufacture, unmarketable, or unlikely to receive marketing approval. We currently generate no revenue from sales of any product and we may never be able to develop or commercialize a marketable product.

We plan to initiate our first clinical trial for our hemoglobinopathy programs in late 2017. Commencing this clinical trial, and any other clinical trials we may initiate, is subject to acceptance by the FDA of our Investigational New Drug application, or IND, and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us to complete additional preclinical studies or we are required to satisfy other FDA requests, the start of our first clinical trial for our hemoglobinopathy programs or any of our other programs may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence our clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect.

Our product candidates will require additional preclinical and clinical development, regulatory and marketing approval in multiple jurisdictions, obtaining manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. In addition, our product development programs must be approved for marketing by the FDA, or certain other foreign regulatory agencies, including the EMA, before we may commercialize our product candidates.

The success of our product candidates will depend on several factors, including the following:

- successful information of product candidates in our development programs;
- successful completion of preclinical studies;
- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials;
- ability to develop safe and effective delivery mechanisms for our *in vivo* therapeutic programs;
- ability to identify optimal RNA sequences to guide genomic editing;
- entry into collaborations to further the development of our product candidates;

- a positive recommendation of the Recombinant DNA Advisory Committee of the U.S. National Institutes of Health, or NIH;
- approval of INDs for our product candidates to commence clinical trials;
- successful enrollment in, and completion of, preclinical studies and clinical trials;
- successful data from our clinical program that supports an acceptable risk-benefit profile of our product candidates in the intended populations;
- receipt of regulatory and marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers for clinical supply and commercial manufacturing and, where applicable, commercial manufacturing capabilities;
- successful development of our internal manufacturing processes and transfer to larger-scale facilities operated by either a contract manufacturing organization, or CMO, or by us;
- establishment and maintenance of patent and trade secret protection or regulatory exclusivity for our product candidates;
- commercial launch of our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of the product candidates, if and when approved, by patients, the medical community and third-party payors;
- effective competition with other therapies and treatment options;
- establishment and maintenance of healthcare coverage and adequate reimbursement;
- enforcement and defense of intellectual property rights and claims;
- maintenance of a continued acceptable safety profile of the product candidates following approval; and
- achieving desirable medicinal properties for the intended indications.

Additionally, because our technology involves gene editing across multiple cell and tissue types, we are subject to many of the challenges and risks that gene therapies face, including:

- regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future; to date, no products that involve the genetic modification of patient cells have been approved in the United States and only one gene therapy product has been approved in the European Union;
- improper insertion of a gene sequence into a patient's chromosome could lead to lymphoma, leukemia or other cancers, or other aberrantly functioning cells; and
- the FDA recommends a follow-up observation period of 15 years or longer for all patients who receive treatment using gene therapies, and we may need to adopt such an observation period for our product candidates.

If we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

Our CRISPR/Cas9 Gene Editing Product Candidates Are Based On A New Gene Editing Technology, Which Makes It Difficult To Predict The Time And Cost Of Development And Of Subsequently Obtaining Regulatory Approval, If At All. There Have Only Been A Limited Number Of Clinical Trials Of Product Candidates Based On Gene Editing Technology And No Gene Editing Products Have Been Approved In The United States Or In The European Union.

CRISPR/Cas9 gene editing technology is relatively new and no products based on CRISPR/Cas9 or other similar gene editing technologies have been approved in the United States or the European Union and only a limited number of clinical trials of products based on gene editing technologies have been commenced, and none have been completed. As such it is difficult to accurately predict the developmental challenges we may incur for our product candidates as they proceed through product discovery or identification, preclinical studies and clinical trials. In addition, because our programs are all in the research or preclinical stage, we have not yet been able to assess safety in humans, and there may be long-term effects from treatment with any of our future product candidates that we cannot predict at this time. Any product candidates we may develop will act at the level of DNA, and, because animal DNA differs from human DNA, testing of our product candidates in animal models may not be predictive of the results we observe in human clinical trials of our product candidates for either safety or efficacy. Also, animal models may not exist for some of the diseases we choose to pursue in our programs. As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our gene editing technology, or any similar or competitive gene editing technologies, will result in the identification, development, and regulatory approval of any products. There can be no assurance that any development problems we experience in the future related to our gene editing technology or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

The clinical trial requirements of the FDA, the EMA and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the product candidate. No products based on gene editing technologies have been approved by regulators. As a result, the regulatory approval process for product candidates such as ours is uncertain and may be more expensive and take longer than the approval process for product candidates based on other, better known or more extensively studied technologies. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or the European Union or how long it will take to commercialize our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product candidate to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects may be harmed.

The FDA, The NIH And The EMA Have Demonstrated Caution In Their Regulation Of Gene Therapy Treatments, And Ethical And Legal Concerns About Gene Therapy And Genetic Testing May Result In Additional Regulations Or Restrictions On The Development And Commercialization Of Our Product Candidates, Which May Be Difficult To Predict.

The FDA, NIH and the EMA have each expressed interest in further regulating biotechnology, including gene therapy and genetic testing. For example, the EMA advocates a risk-based approach to the development of a gene therapy product. Agencies at both the federal and state level in the United States, as well as U.S. congressional committees and foreign governments, have also expressed interest in further regulating the biotechnology industry. Such action may delay or prevent commercialization of some or all of our product candidates. Within the broader genome product field, only one gene therapy product, uniQure N.V.'s Glybera, has received marketing authorization from the European Commission, and no gene therapy products have received marketing approval in the United States.

Regulatory requirements in the United States and abroad governing gene therapy products have changed frequently and may continue to change in the future. The FDA established the Office of Cellular, Tissue and

Gene Therapies within its Center for Biologics Evaluation and Research to consolidate the review of gene therapy and related products, and established the Cellular, Tissue and Gene Therapies Advisory Committee to advise this review. Prior to submitting an IND, our human clinical trials are subject to review by the NIH Office of Biotechnology Activities, or OBA, Recombinant DNA Advisory Committee, or the RAC. Following an initial review, RAC members make a recommendation as to whether the protocol raises important scientific, safety, medical, ethical or social issues that warrant in-depth discussion at the RAC's quarterly meetings. Even though the FDA decides whether individual gene therapy protocols may proceed under an IND, the RAC's recommendations are shared with the FDA and the RAC public review process, if undertaken, can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and has not objected to its initiation or has notified the sponsor that the study may begin. Conversely, the FDA can put an IND on a clinical hold even if the RAC has provided a favorable review or has recommended against an in-depth, public review. Moreover, under guidelines published by the NIH, patient enrollment in our future gene editing clinical trials cannot begin until the investigator for such clinical trial has received a letter from the OBA indicating that the RAC review process has been completed; and Institutional Biosafety Committee, or IBC, approval as well as all other applicable regulatory authorizations have been obtained. In addition to the government regulators, the IBC and institutional review board, or IRB, of each institution at which we conduct clinical trials of our product candidates, or a central IRB if appropriate, would need to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of any of our product candidates. Similarly, the EMA governs the development of gene therapies in the European Union and may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines.

These regulatory review agencies and committees and the new requirements or guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory agencies and committees and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our or our collaborators' ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

If Any Of The Product Candidates We May Develop Or The Delivery Modes We Rely On Cause Undesirable Side Effects, It Could Delay Or Prevent Their Regulatory Approval, Limit The Commercial Potential Or Result In Significant Negative Consequences Following Any Potential Marketing Approval.

Product candidates we may develop may be associated with undesirable side effects, unexpected characteristics or other serious adverse events, including off-target cuts of DNA, or the introduction of cuts in DNA at locations other than the target sequence. These off-target cuts could lead to disruption of a gene or a genetic regulatory sequence at an unintended site in the DNA, or, in those instances where we also provide a segment of DNA to serve as a repair template, it is possible that following off-target cut events, DNA from such repair template could be integrated into the genome at an unintended site, potentially disrupting another important gene or genomic element. There also is the potential risk of delayed adverse events following exposure to gene editing therapy due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material. Possible adverse side effects that could occur with treatment with gene editing products include an immunologic reaction after administration which could substantially limit the effectiveness of the treatment. If our CRISPR/Cas9 gene editing technology demonstrates a similar effect, we may decide or be required to halt or delay preclinical development or clinical development of our product candidates. In addition to serious adverse events or side effects caused by any product candidate we may develop, the administration process or related procedures also can cause undesirable side effects. If any such events occur, our clinical trials could be suspended or terminated.

If in the future we are unable to demonstrate that such adverse events were caused by factors other than our product candidate, the FDA, EMA or other comparable foreign regulatory authorities could order us to cease further clinical studies of, or deny approval of, any product candidates we are able to develop for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any product candidate we may develop, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to identify and develop product candidates, and may harm our business, financial condition, result of operations and prospects significantly.

Additionally, if we successfully develop a product candidate and it receives marketing approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy, or REMS, to ensure that the benefits of treatment with such product candidate outweighs the risks for each potential patient, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients, a communication plan to health care practitioners, extensive patient monitoring, or distribution systems and processes that are highly controlled, restrictive, and more costly than what is typical for the industry. Furthermore, if we or others later identify undesirable side effects caused by any product candidate that we to develop, several potentially significant negative consequences could result, including:

- regulatory authorities may revoke licenses or suspend, vary or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our CRISPR/Cas9 technology and any product candidates we may identify and develop and could have a material adverse effect on our business, financial condition, results of operations and prospects.

If We Experience Delays Or Difficulties In The Enrollment Of Patients In Clinical Trials, Our Receipt Of Necessary Regulatory Approvals Could Be Delayed Or Prevented.

We or our collaborators may not be able to initiate or continue clinical trials for any product candidates we identify or develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or analogous regulatory authorities outside the United States, or as needed to provide appropriate statistical power for a given trial. Enrollment may be particularly challenging for any rare genetically defined diseases we may target in the future. In addition, if patients are unwilling to participate in our gene editing trials because of negative publicity from adverse events related to the biotechnology, gene therapy or gene editing fields, competitive clinical trials for similar patient populations, clinical trials in competing products, or for other reasons, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of any product candidates we may develop may be delayed. Moreover, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as any product candidates we may develop, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;

- size of the patient population and process for identifying subjects;
- design of the trial protocol;
- availability and efficacy of approved medications for the disease under investigation;
- availability of genetic testing for potential patients;
- ability to obtain and maintain subject consent;
- risk that enrolled subjects will drop out before completion of the trial;
- eligibility and exclusion criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial;
- perceived risks and benefits of gene editing and cellular therapies as therapeutic approaches;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Enrollment delays in our clinical trials may result in increased development costs for any product candidates we may develop, which would cause the value of our Company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit, or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business, financial condition, results of operations, and prospects.

Positive Results From Early Preclinical Studies Of Our Product Candidates Are Not Necessarily Predictive Of The Results Of Later Preclinical Studies And Any Future Clinical Trials Of Our Product Candidates. If We Cannot Replicate The Positive Results From Our Earlier Preclinical Studies Of Our Product Candidates In Our Later Preclinical Studies And Future Clinical Trials, We May Be Unable To Successfully Develop, Obtain Regulatory Approval For And Commercialize Our Product Candidates.

Any positive results from our preclinical studies of our product candidates may not necessarily be predictive of the results from required later preclinical studies and clinical trials. Similarly, even if we are able to complete our planned preclinical studies or any future clinical trials of our product candidates according to our current development timeline, the positive results from such preclinical studies and clinical trials of our product candidates may not be replicated in subsequent preclinical studies or clinical trial results.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, non-clinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or EMA approval.

Even If We Complete The Necessary Preclinical Studies And Clinical Trials, The Marketing Approval Process Is Expensive, Time-Consuming, And Uncertain And May Prevent Us From Obtaining Approvals For The Commercialization Of Any Product Candidates We May Develop. If We Are Not Able To Obtain,

Or If There Are Delays In Obtaining, Required Regulatory Approvals, We Will Not Be Able To Commercialize, Or Will Be Delayed In Commercializing, Product Candidates We May Develop, And Our Ability To Generate Revenue Will Be Materially Impaired.

Any product candidates we may develop and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval or clearance to market any product candidates from regulatory authorities in any jurisdiction and it is possible that none of our product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval or clearance. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations, or CROs, or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the biologic product candidate's safety, purity, efficacy and potency. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any product candidates we develop may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of any product candidates we may develop, the commercial prospects for those product candidates may be harmed, and our ability to generate revenues will be materially impaired.

We May Never Obtain FDA Approval For Any Of Our Product Candidates In The United States, And Even If We Do, We May Never Obtain Approval For Or Commercialize Any Of Our Product Candidates In Any Other Jurisdiction, Which Would Limit Our Ability To Realize Their Full Market Potential.

In order to eventually market any of our product candidates in any particular foreign jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a jurisdiction-by-jurisdiction basis regarding safety and efficacy. Approval by the FDA in the United States, if obtained, does not ensure approval by regulatory authorities in other countries or jurisdictions. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional preclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. The foreign regulatory approval process involves all of the risks associated with FDA approval. We do not have any product candidates approved

for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be unrealized.

Gene editing Products Are Novel And May Be Complex And Difficult To Manufacture. We Could Experience Manufacturing Problems That Result In Delays In The Development Or Commercialization Of Our Product Candidates Or Otherwise Harm Our Business.

The manufacturing process used to produce CRISPR/Cas9-based product candidates may be complex, as they are novel and have not been validated for clinical and commercial production. Several factors could cause production interruptions, including equipment malfunctions, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error or disruptions in the operations of our suppliers.

Our product candidates will require processing steps that are more complex than those required for most small molecule drugs. Moreover, unlike small molecules, the physical and chemical properties of biologics generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Accordingly, we will employ multiple steps to control the manufacturing process to assure that the process works and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical grade materials that meet FDA, the EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA, the EMA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA or other foreign regulatory authorities may require that we not distribute a lot until the relevant agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects. Problems in our manufacturing process could restrict our ability to meet market demand for our products.

We also may encounter problems hiring and retaining the experienced scientific, quality-control and manufacturing personnel needed to operate our manufacturing processes, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements. Any problems in our manufacturing process or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs.

Adverse Public Perception Of Gene Editing And Cellular Therapy Products May Negatively Impact Demand For, Or Regulatory Approval Of, Our Product Candidates.

Our product candidates involve editing the human genome. The clinical and commercial success of our product candidates will depend in part on public acceptance of the use of gene editing therapies for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene editing is unsafe, unethical, or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Negative public reaction to gene therapy in general could result in greater government regulation and stricter labeling requirements of gene editing products, including any of our product candidates,

and could cause a decrease in the demand for any products we may develop. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

If, In The Future, We Are Unable To Establish Sales And Marketing Capabilities Or Enter Into Agreements With Third Parties To Sell And Market Products Based On Our Technologies, We May Not Be Successful In Commercializing Our Products If And When Any Products Candidates Are Approved And We May Not Be Able To Generate Any Revenue.

We do not currently have a sales or marketing infrastructure and, as a company, have no experience in the sale, marketing or distribution of therapeutic products. To achieve commercial success for any approved product candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future product that we may develop;
- the lack of complementary treatments to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability to us from these revenue streams is likely to be lower than if we were to market and sell any product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we may not be successful in commercializing our product candidates. Further, our business, results of operations, financial condition and prospects will be materially adversely affected.

In particular, gene editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns relating to the application of gene editing technology to human embryos or the human germline. For example, in April 2015, Chinese scientists reported on their attempts to edit the genome of human embryos to modify the gene for hemoglobin beta. This is the gene in which a mutation occurs in patients with the inherited blood disorder beta-thalassemia. Although this research was purposefully conducted in embryos that were not viable, the work prompted calls for a moratorium or other types of restrictions on gene editing of human eggs, sperm, and embryos. The Alliance for Regenerative Medicine in Washington has called for a voluntary moratorium on the use of gene editing technologies, including CRISPR/Cas9, in research that involved altering

human embryos or human germline cells. Similarly, the NIH has announced that it would not fund any use of gene editing technologies in human embryos, noting that there are multiple existing legislative and regulatory prohibitions against such work, including the Dickey-Wicker Amendment, which prohibits the use of appropriated funds for the creation of human embryos for research purposes or for research in which human embryos are destroyed. Laws in the United Kingdom prohibit genetically modified embryos from being implanted into women, but embryos can be altered in research labs under license from the Human Fertilisation and Embryology Authority. Research on embryos is more tightly controlled in many other European countries.

Although we do not use our technologies to edit human embryos or the human germline, such public debate about the use of gene editing technologies in human embryos and heightened regulatory scrutiny could prevent or delay our development of product candidates. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair our development and commercialization of product candidates or demand for any products we may develop. Adverse events in our preclinical studies or clinical trials or those of our competitors or of academic researchers utilizing gene editing technologies, even if not ultimately attributable to product candidates we may identify and develop, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of potential product candidates we may identify and develop, stricter labeling requirements for those product candidates that are approved, and a decrease in demand for any such product candidates.

Even If We, Or Any Collaborators We May Have, Obtain Marketing Approvals For Any Product Candidates We Develop, The Terms Of Approvals And Ongoing Regulation Of Our Products Could Require The Substantial Expenditure Of Resources And May Limit How We, Or They, Manufacture And Market Our Products, Which Could Materially Impair Our Ability To Generate Revenue.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising, and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, current Good Manufacturing Practice, or cGMP, requirements relating to quality control, quality assurance and corresponding maintenance of records and documents and requirements regarding recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA also may place other conditions on approvals including the requirement for a REMS to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the Biologics License Application, or BLA, must submit a proposed REMS before it can obtain approval. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more product candidates we develop, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, and quality control. If we and such collaborators are not able to comply with post-approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition, and prospects.

Any Product Candidate For Which We Obtain Marketing Approval Could Be Subject To Restrictions Or Withdrawal From The Market, And We May Be Subject To Substantial Penalties If We Fail To Comply With Regulatory Requirements Or If We Experience Unanticipated Problems With Our Products, When And If Any Of Them Are Approved.

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of biologics to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice. Violation of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown problems with a product candidate, including adverse events of unanticipated severity or frequency, or with our manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on such products, manufacturers, or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on the distribution or use of a product;
- requirements to conduct post-marketing clinical trials;
- receipt of warning or untitled letters;
- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory biologic recalls;
- refusal to approve pending applications or supplements to approved applications that we submit;
- fines, restitution, or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals or revocation of biologics licenses;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our products;
- product seizure or detention; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may also inhibit our ability to commercialize any product candidates we may develop and adversely affect our business, financial condition, results of operations, and prospects.

The Commercial Success Of Any Of Our Product Candidates Will Depend Upon Its Degree Of Market Acceptance By Physicians, Patients, Third-party Payors And Others In The Medical Community.

Ethical, social and legal concerns about gene therapy could result in additional regulations restricting or prohibiting our products. Even with the requisite approvals from FDA in the United States, the EMA in the European Union and other regulatory authorities internationally, the commercial success of our product candidates will depend, in part, on the acceptance of physicians, patients and health care payors of gene therapy products in general, and our product candidates in particular, as medically necessary, cost-effective and safe. Any product that we commercialize may not gain acceptance by physicians, patients, health care payors and others in the medical community. The degree of market acceptance of gene therapy products and, in particular, our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy, durability and safety of such product candidates as demonstrated in any future clinical trials;
- the potential and perceived advantages of product candidates over alternative treatments;
- the cost of treatment relative to alternative treatments;
- the clinical indications for which the product candidate is approved by FDA or the EMA;
- patient awareness of, and willingness to seek, genotyping;
- the willingness of physicians to prescribe new therapies;
- the willingness of the target patient population to try new therapies;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of FDA, the EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- relative convenience and ease of administration;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party payor coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and future clinical trials, market acceptance of the product will not be fully known until after it is launched. If our product candidates do not achieve an adequate level of acceptance following regulatory approval, if ever, we may not generate significant product revenue and may not become profitable.

We May Expend Our Limited Resources To Pursue A Particular Product Candidate Or Indication And Fail To Capitalize On Product Candidates Or Indications That May Be More Profitable Or For Which There Is A Greater Likelihood Of Success.

We have limited financial and managerial resources. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to timely capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We Face Significant Competition In An Environment Of Rapid Technological Change And The Possibility That Our Competitors May Achieve Regulatory Approval Before Us Or Develop Therapies That Are More Advanced Or Effective Than Ours, Which May Harm Our Business And Financial Condition, And Our Ability To Successfully Market Or Commercialize Our Product Candidates.

The biotechnology and pharmaceutical industries, including the gene therapy field, are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions, some or all of which may have greater access to capital or resources than we do.

We are aware of several companies focused on developing gene editing in various indications using CRISPR/Cas9 gene editing technology, including Intellia Therapeutics, Inc. and Editas Medicine, Inc., or Editas. There can be no certainty that other gene editing technologies will not be considered better or more attractive than our technology for the development of products. For example, researchers, including Feng Zhang, Ph.D., one of the founders of Editas recently announced the discovery of a CRISPR system involving a different protein, Cpf1, which can also edit human DNA. These researchers have asserted that Cpf1 may work better than Cas9 in some cases. Cas9 may be determined to be less attractive than Cpf1 or other CRISPR proteins that have yet to be discovered.

There are additional companies developing therapies using additional gene editing technologies, including transcription activator-like effector nucleases (TALENs), meganucleases and zinc finger nucleases (ZFNs). These companies include bluebird bio, Cellectis, Poseida Therapeutics, Precision Biosciences, and Sangamo Biosciences. Additional companies developing gene therapy products include Abeona Therapeutics, Avalanche Biotechnologies, Dimension Therapeutics, REGENXBIO, Spark Therapeutics and uniQure. In addition to competition from other gene editing therapies or gene therapies, any product we may develop may also face competition from other types of therapies, such as small molecule, antibody or protein therapies. In addition, new scientific discoveries may cause CRISPR/Cas9 technology, or gene editing as a whole, to be considered an inferior form of therapy.

Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical studies, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology, and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop or that would render any products that we may develop obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors' products and our patents may not be sufficient to prevent our competitors from commercializing competing products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

To become and remain profitable, we must develop and eventually commercialize product candidates with significant market potential, which will require us to be successful in a range of challenging activities. These activities can include completing preclinical studies and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products that are approved and satisfying any post marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our Company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our Company also could cause you to lose all or part of your investment.

Even If We Are Able To Commercialize Any Product Candidates, Such Products May Become Subject To Unfavorable Pricing Regulations, Third-party Reimbursement Practices, Or Healthcare Reform Initiatives, Which Would Harm Our Business.

The regulations that govern marketing approvals, pricing, and reimbursement for new biologic products vary widely from country to country. In the United States, recently enacted legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

Our ability to commercialize any products successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment

limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

Risks Related to Our Relationships with Third Parties

If Conflicts Arise Between Us And Our Collaborators Or Strategic Partners, These Parties May Act In A Manner Adverse To Us And Could Limit Our Ability To Implement Our Strategies.

If conflicts arise between our corporate or academic collaborators or strategic partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Some of our academic collaborators and strategic partners are conducting multiple product development efforts within each area that is the subject of the collaboration with us. Our collaborators or strategic partners, however, may develop, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for our product candidates.

Some of our collaborators or strategic partners could also become our competitors in the future. Our collaborators or strategic partners could develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, or fail to devote sufficient resources to the development and commercialization of products. Any of these developments could harm our product development efforts.

Our Collaborators And Strategic Partners May Control Aspects Of Our Clinical Trials, Which Could Result In Delays And Other Obstacles In The Commercialization Of Our Proposed Products And Materially Harm Our Results Of Operations.

For some programs, we will depend on third party collaborators and strategic partners to design and conduct our clinical trials. As a result, we may not be able to conduct these programs in the manner or on the time schedule we currently contemplate, which may negatively impact our business operations. In addition, if any of these collaborators or strategic partners withdraw support for our programs or proposed products or otherwise impair their development, our business could be negatively affected.

In October 2015, we entered into a four-year collaboration agreement with Vertex to research, develop and commercialize new treatments aimed at the underlying genetic causes of human diseases, including beta-thalassemia and sickle cell. In addition, in December 2015, we entered into an agreement with Bayer Healthcare to create a joint venture to discover and commercialize therapeutics for the treatment of blood disorders, blindness and congenital heart disease based on our CRISPR/Cas9 gene editing technology.

We and Bayer Healthcare each hold a 50% interest in the joint venture and each have two designees on the management board. As such, we cannot control all aspects of the clinical development and commercialization of any product candidate developed by the joint venture. Similarly, under our collaboration agreement with Vertex, Vertex has sole authority to select genetic targets to pursue and we will not have control over the development of any product candidates. Our lack of control over the clinical development in our agreements with Bayer Healthcare and Vertex could cause delays or other difficulties in the development and commercialization of our product candidates, which may prevent us from completing the intended IND filings in a timely fashion, if at all.

In addition, the termination of either our agreement with Bayer Healthcare or Vertex would prevent us from receiving any milestone, royalty payments and other benefits under these agreements and would have a materially adverse effect on our results of operations.

Our Collaborators Or Strategic Partners May Decide To Adopt Alternative Technologies Or May Be Unable To Develop Commercially Viable Products With Our Technology, Which Would Negatively Impact Our Revenues And Our Strategy To Develop These Products.

Our collaborators or strategic partners may adopt alternative technologies, which could decrease the marketability of our CRISPR/Cas9 gene editing technology. Additionally, because our current or future collaborators or strategic partners are likely to be working on more than one development project, they could choose to shift their resources to projects other than those they are working on with us. If they do so, this would delay our ability to test our technology and would delay or terminate the development of potential products based on our CRISPR/Cas9 gene editing technology. Further, our collaborators and strategic partners may elect not to develop products arising out of our collaborative and strategic partnering arrangements or to devote sufficient resources to the development, manufacturing, marketing or sale of these products. The failure to develop and commercialize a product candidate pursuant to our agreements with our current or future collaborators would prevent us from receiving future milestone and royalty payments which would negatively impact our revenues.

We May Seek To Establish Additional Collaborations And, If We Are Not Able To Establish Them On Commercially Reasonable Terms, We May Have To Alter Our Development And Commercialization Plans.

Our product candidate development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for any additional collaborations will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. For example, we have granted exclusive rights to Vertex for certain genetic targets, and during the term of the collaboration agreement, we will be restricted from granting rights to other parties to use our CRISPR/Cas9 technology to pursue therapies that address these genetic targets. Similarly, pursuant to our joint venture agreement with Bayer Healthcare, during the term of the joint venture, and for a specified period after the termination of the joint venture, we will be prohibited from developing products that use our CRISPR/Cas9 technology in specified fields that would compete with the joint venture and Bayer Healthcare, respectively. The non-competition provisions in each of these agreements could limit our ability to enter into strategic collaborations with future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. If we are unable to negotiate and enter into new collaborations, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay

its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

We May Rely On Third Parties To Conduct Our Preclinical Studies And Any Future Clinical Trials For Our Product Candidates. If These Third Parties Do Not Successfully Carry Out Their Contractual Duties, Comply With Regulatory Requirements Or Meet Expected Deadlines, We May Not Be Able To Obtain Regulatory Approval For Or Commercialize Our Product Candidates And Our Business Could Be Substantially Harmed.

We may rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct preclinical studies and future clinical trials for our product candidates. Nevertheless, we will be responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards and our reliance on CROs will not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with regulations, commonly referred to as Good Clinical Practices, or GCPs, for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions. For any violations of laws and regulations during the conduct of our preclinical studies and clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

We and our CROs will be required to comply with regulations, including GCPs, for conducting, monitoring, recording and reporting the results of preclinical studies and clinical trials to ensure that the data and results are scientifically credible and accurate and that the trial patients are adequately informed, among other things, of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any drugs in clinical development. The FDA enforces GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our future clinical trials will comply with GCPs. In addition, our future clinical trials must be conducted with product candidates produced in accordance with the requirements in cGMP regulations. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action.

Although we intend to design the clinical trials for our product candidates, CROs will conduct all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future preclinical studies and clinical trials will also result in less direct control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;

- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical studies and clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs do not perform preclinical studies and future clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our product candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our product candidates, or our development programs may be materially and irreversibly harmed. If we are unable to rely on preclinical and clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct and this could significantly delay commercialization and require significantly greater expenditures.

We Expect To Rely On Third Parties To Manufacture Our Clinical Product Supplies, And We Intend To Rely On Third Parties For At Least A Portion Of The Manufacturing Process Of Our Product Candidates, If Approved. Our Business Could Be Harmed If The Third Parties Fail To Provide Us With Sufficient Quantities Of Product Inputs Or Fail To Do So At Acceptable Quality Levels Or Prices.

We do not currently own any facility that may be used as our clinical-scale manufacturing and processing facility and must eventually rely on outside vendors to manufacture supplies and process our product candidates. We have not yet caused any product candidates to be manufactured or processed on a commercial scale and may not be able to do so for any of our product candidates. We will make changes as we work to optimize the manufacturing process, and we cannot be sure that even minor changes in the process will result in therapies that are safe and effective.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA or other foreign regulatory agencies pursuant to inspections that will be conducted after we submit an application to the FDA or other foreign regulatory agencies. We will not control the manufacturing process of, and will be completely dependent on, our contract manufacturing partners for compliance with regulatory requirements, known as cGMP requirements, for manufacture of our product candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

Our Relationships With Healthcare Providers, Physicians, And Third-party Payors Will Be Subject To Applicable Anti-kickback, Fraud And Abuse And Other Healthcare Laws And Regulations, Which Could Expose Us To Criminal Sanctions, Civil Penalties, Exclusion From Government Healthcare Programs, Contractual Damages, Reputational Harm And Diminished Profits And Future Earnings.

Although we do not currently have any drugs on the market, once we begin commercializing our product candidates, if ever, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates that we may develop for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our product candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order, or recommendation of, any good or service, for which payment may be made under a state or Federal healthcare program, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violation of the statute may give rise to criminal and/or civil penalties;
- the federal civil and criminal false claims laws, including the civil False Claims Act, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid, or other government payors that are false, fictitious or fraudulent or knowingly making, using or causing to be made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $5,500 to $11,000 per false claim. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false of fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as further amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations which impose certain requirements on covered entities, including healthcare providers, health plans and healthcare clearing houses, as well as their business associates that perform certain services with respect to safeguarding the privacy, security and transmission of individually identifiable health information that constitutes protected health information, including mandatory contractual terms and restrictions on the use and/or disclosure of such information without appropriate authorization;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal physician payment transparency requirements, sometimes referred to as the “Sunshine Act” under the Affordable Care Act, require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program to report to the Department of Health and Human Services information related to physician payments and other transfers of value to physicians and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of

such laws. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization, and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales team, are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs. Liabilities they incur pursuant to these laws could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business

Our Future Success Depends On Our Ability To Retain Key Executives And To Attract, Retain And Motivate Qualified Personnel.

We are highly dependent on the research and development, clinical, commercial and business development expertise of Dr. Rodger Novak, our President and Chief Executive Officer, Dr. Sven Ante (Bill) Lundberg, our Chief Scientific Officer, Dr. Samarth Kulkarni, our Chief Business Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment letter agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. The loss of the services of our executive officers or other key employees or consultants could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. If we are unable to retain high quality personnel, our ability to pursue our growth strategy will be limited.

We will also need to recruit and retain qualified scientific and clinical personnel as we advance the development of our product candidates and product pipeline. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

In addition, being organized in Switzerland may restrict our ability to attract, motivate and retain the required level of qualified personnel. In Switzerland, new legislation affecting public companies has been passed that, among other things, (i) imposes an annual binding shareholders' "say on pay" vote with respect to the compensation of executive management, including executive officers and the board of directors; (ii) prohibits severance, advances, transaction premiums and similar payments to executive officers and directors; and (iii) requires companies to specify various compensation-related matters in their articles of association, thus requiring them to be approved by a shareholders' vote.

We Will Need To Develop And Expand Our Company, And We May Encounter Difficulties In Managing This Development And Expansion, Which Could Disrupt Our Operations.

As of April 30, 2016, we had 55 full-time employees and, in connection with becoming a public company, we expect to increase our number of employees and the scope of our operations. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our Company.

Our Employees, Principal Investigators, Consultants And Commercial Partners May Engage In Misconduct Or Other Improper Activities, Including Non-compliance With Regulatory Standards And Requirements And Insider Trading.

We are exposed to the risk of fraud or other misconduct by our employees, consultants, and commercial partners, and, if we commence clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the European Commission, and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We intend to adopt, prior to the completion of this offering, a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may

not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations, and prospects, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

If We Fail To Comply With Environmental, Health And Safety Laws And Regulations, We Could Become Subject To Fines Or Penalties Or Incur Costs That Could Harm Our Business.

We will become subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations will involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also may produce hazardous waste products. We generally anticipate contracting with third parties for the disposal of these materials and wastes. We will not be able to eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from any use by us of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological or hazardous materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Product Liability Lawsuits Against Us Could Cause Us To Incur Substantial Liabilities And Could Limit Commercialization Of Any Product Candidates That We May Develop.

We will face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any product candidates that we may develop. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any product candidates that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage when we begin clinical trials and if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

If We Fail To Establish And Maintain Proper And Effective Internal Control Over Financial Reporting, Our Operating Results And Our Ability To Operate Our Business Could Be Harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. In connection with this offering, we intend to begin the process of documenting, reviewing and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act of 2002, or SOX, which will require annual management assessment of the effectiveness of our internal control over financial reporting. We have begun recruiting additional finance and accounting personnel with certain skill sets that we will need as a public company.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our common share price and make it more difficult for us to effectively market and sell our service to new and existing customers.

Our Internal Computer Systems, Or Those Of Our Collaborators Or Other Contractors Or Consultants, May Fail Or Suffer Security Breaches, Which Could Result In A Material Disruption Of Our Product Development Programs.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

Our Business Is Subject To Economic, Political, Regulatory And Other Risks Associated With International Operations.

Our business is subject to risks associated with conducting business internationally. We and a number of our suppliers and collaborative and clinical study relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;

- differing regulatory requirements for drug approvals in non-U.S. countries;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including floods and fires.

Risks Related to Intellectual Property

If We Are Unable To Adequately Protect Our Proprietary Technology Or Obtain And Maintain Patent Protection For The Products We Develop And For Our Technology And Product Candidates, Or If The Scope Of The Patent Protection Obtained Is Not Sufficiently Broad, Our Competitors Could Develop And Commercialize Products And Technology Similar Or Identical To Ours, And Our Ability To Successfully Commercialize Any Product Candidates We May Develop, And Our Technology May Be Adversely Affected.

Our success depends in large part on our ability to obtain and maintain proprietary or intellectual property protection in the United States and other countries with respect to our CRISPR/Cas9 platform technology and any proprietary product candidates and technology we develop. Currently, no patents covering our CRISPR/Cas9 platform or product candidates have been issued to us in the United States and one of the patent applications we have licensed that may cover our platform is the subject of an interference proceeding at the United States Patent and Trademark Office, or USPTO, which is discussed below. We seek to protect our proprietary position by in-licensing intellectual property to cover our platform technology and filing patent applications in the United States and abroad related to our technologies and product candidates that are important to our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position. If we or our licensors are unable to obtain or maintain patent protection with respect to our CRISPR/Cas9 platform technology and any proprietary products and technology we develop, our business, financial condition, results of operations and prospects could be materially harmed.

The scope of patent protection that will be available to us in the United States and in other countries is uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. With respect to both in-licensed and owned intellectual property, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors, or if any such patents will be found invalid, unenforceable or not infringed if challenged by our competitors.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, publications of discoveries in the scientific literature often lag behind the actual discoveries and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with any degree of certainty whether the inventors of our licensed patents and applications were the first to make the inventions claimed in our owned or any licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we license or own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we hold or in-license may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether any of our platform advances and product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. For example, we are aware that third parties have suggested the use of the CRISPR technology in conjunction with a protein other than Cas9. Our owned and in-licensed patents may not cover such technology. If our competitors commercialize the CRISPR technology in conjunction with a protein other than Cas9, our business, financial condition, results of operations, and prospects could be materially adversely affected.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability and our patents may be challenged in the courts or patent offices in the United States and abroad. We may be subject to a third party preissuance submission of prior art to the USPTO or other patent office abroad or become involved in opposition, derivation, revocation, reexamination, post-grant and inter partes review, or interference proceedings challenging our patent rights or the patent rights of others. Indeed, certain of our fundamental intellectual property has been subject to third party observations outside the United States and interference proceedings within the United States. Competitors may claim that they invented the inventions claimed in such issued patents or patent applications prior to our inventors, or may have filed patent applications before our inventors did. A competitor may also claim that our products and services infringe its patents and that we therefore cannot practice our technology as claimed under our patent applications, if issued. An adverse determination in any such claim may result in our inability to manufacture or commercialize products without infringing third-party patent rights. Competitors may also contest our patents, if issued, by showing that the invention was not patent-eligible, was not novel, was obvious or that the patent claims failed any other requirement for patentability. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights or allow third parties to commercialize our technology or products and compete directly with us, without payment to us. Moreover, we, or one of our licensors, may have to participate in additional interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of

patentability. Such challenges may result in loss of patent rights, loss of exclusivity or freedom to operate, or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

We Are Required To Pay Royalties Under Our License Agreements With Third-party Licensors, And We Must Use Commercially Reasonable Diligence Efforts And Meet Milestones To Maintain Our License Rights.

Under our in-license agreements, including our in-license agreements with Dr. Emmanuelle Charpentier, we will be required to pay royalties based on our revenues from sales of our products utilizing the licensed technologies and these royalty payments could adversely affect the overall profitability for us of any products that we may seek to commercialize. Under each of our in-license agreements with, Dr. Charpentier, we have an obligation to use commercially reasonable efforts to develop and obtain regulatory approval to market a licensed therapeutic product. Our in-license agreements with Dr. Charpentier also include an obligation to file a U.S. Investigational New Drug application (or its equivalent in a major market country) by April 2021 and an obligation to file a U.S. Investigational New Drug application (or its equivalent in a major market country) by April 2024. We may not be successful in meeting these obligations in the future on a timely basis or at all. Our failure to meet these obligations may give Dr. Charpentier the right to terminate our license rights. We will need to outsource and rely on third parties for many aspects of the clinical development of the products covered under our license agreements. Delay or failure by these third parties could adversely affect our ability to meet our diligence obligations and the continuation of our license agreements with third-party licensors.

Some Of Our In-licensed Patent Applications Are Subject To Priority Disputes And Inventorship Disputes, Including An Active Interference Proceeding With The Broad Institute And MIT, In Front Of The United States Patent And Trademark Office. In Addition, Our Owned And In-Licensed Patents And Other Intellectual Property May Be Subject To Further Priority Disputes Or To Inventorship Disputes And Similar Proceedings. If We Or Our Licensors Are Unsuccessful In Any Of These Proceedings, We May Be Required To Obtain Licenses From Third Parties, Which May Not Be Available On Commercially Reasonable Terms Or At All, Or To Cease The Development, Manufacture, And Commercialization Of One Or More Of The Product Candidates We May Develop, Which Could Have A Material Adverse Impact On Our Business.

In January 2016, at our request, the USPTO declared an interference between one of the pending U.S. patent applications we licensed from Dr. Emmanuelle Charpentier and twelve issued U.S. patents, and subsequently added one U.S. patent application, owned jointly by the Broad Institute and Massachusetts Institute of Technology and, in some instances, the President and Fellows of Harvard College, collectively referred to as the Broad. An interference is a proceeding conducted at the USPTO by the Patent Trial and Appeal Board, or PTAB, to determine which party was the first to invent subject matter claimed by both of these parties. There are currently two parties to this interference. Because our application was filed first, the USPTO designated Dr. Charpentier, the Regents of the University of California, or California, and the University of Vienna, or Vienna, collectively as “Senior Party” and designated Broad as “Junior Party.” Following motions by the parties and, potentially, a determination regarding which of the two parties was the first to invent, all of which would happen within the next several months, the PTAB might conclude that the contested subject matter is not patentable to the Senior Party and is patentable to the Junior Party, which in this case could preclude our U.S. patent applications from issuing as patents, in which case the proceedings would result in our losing the right to protect core innovations and our freedom to practice our core gene editing technology. If that happens, it would materially harm our business. Other outcomes could be more favorable to us. They include a determination that

the contested subject matter is patentable to the Senior Party and not patentable to the Junior Party, which in this case could result in the cancellation of some or all of Broad's claims. Intermediate outcomes could also occur, including a determination that the contested subject matter is not patentable to either party, or that the interference should be dismissed. Either party can appeal an adverse decision to the U.S. Court of Appeals for the Federal Circuit. In any case, it may be years before there is a final determination on priority.

Furthermore, we may be involved in further interference proceedings or other disputes in the future. For example, ToolGen Inc., or ToolGen, filed Suggestions of Interference in the USPTO on April 13, 2015, and December 3, 2015, suggesting that they believe some of the claims in pending U.S. applications owned by ToolGen (U.S. Serial No. 14/685,568 and U.S. Serial No. 14/685,510, respectively) interfere with certain claims in five of the Broad patents currently involved in the interference with Dr. Emmanuelle Charpentier, California and Vienna. The USPTO may, in the future, declare an interference between our patent application and one or more ToolGen patent applications. We are also aware of additional third parties that have pending patent applications relating to CRISPR technologies, which similarly may or may not lead to further interference proceedings. For example, Rockefeller University has filed a continuation application (U.S. Serial No. 14/324,960) of an application filed by the Broad, but which names Rockefeller's employee Luciano Marraffini as co-inventor of CRISPR/Cas9 technology; Vilnius University has filed applications in the United States and abroad (published internationally as WO2013/141680 and WO2013/142578), Harvard University has filed applications in the United States and abroad (published internationally as WO2014/099744), and Sigma-Aldrich has filed applications in the United States and abroad (published internationally as WO2014/089290), each claiming aspects of CRISPR/Cas9 technology based on applications claiming priority to provisional filings in 2012. Numerous other filings are based on provisional applications filed after 2012.

Similarly, our intellectual property may in the future become involved in opposition proceedings in Europe or other foreign jurisdictions.

If we or our licensors are unsuccessful in any interference proceedings or other priority or validity disputes (including any patent oppositions) to which we or they are subject or become subject to, we may lose valuable intellectual property rights through the loss or narrowing of one or more of our patent applications. If we or our licensors are unsuccessful in any interference proceeding or other dispute, we may be required to seek to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other disputes. These third parties would be under no obligation to grant to us any such license and such licenses may not be available on commercially reasonable terms or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we and our partners may need to cease the practice of our core gene editing, and the development, manufacture, and commercialization of one or more of the product candidates we may develop. The loss of exclusivity or the narrowing of our patent claims could limit our ability to stop others from using or commercializing similar or identical technology and products. Any of the foregoing could result in a material adverse effect on our business, financial condition, results of operations, or prospects. If we are unsuccessful in the interference proceedings with Broad, we and our partners may be blocked from commercializing any products based on our core gene editing technology. Even if we are successful in an interference proceeding or other similar disputes, it could result in substantial costs and be a distraction to management and other employees.

The Intellectual Property That Protects Our Core Gene editing Technology Is Jointly Owned, And Our License Is From Only One Of The Joint Owners, Materially Limiting Our Rights In The United States And Abroad.

The family of patent applications we have in-licensed from Dr. Emmanuelle Charpentier is the foundational patent protection for our core gene editing technology. However, that family includes other named inventors who assigned their rights either to California or to Vienna. As such, the intellectual property is currently co-owned by Dr. Charpentier, California, and Vienna. Although we have in-licensed Dr. Charpentier's rights to the intellectual property, we do not have a license to California or Vienna's rights to the intellectual property. As explained more fully below, that leaves us in a position of holding only non-exclusive rights to the patent rights that protect our core gene editing technology.

In the absence of an agreement among co-owners, jointly owned patent rights are subject to default rules pertaining to the rights and obligations of joint owners, which vary by jurisdiction, and in some countries we may not even have valid non-exclusive rights to that technology. For example, some countries, in particular European countries, require the consent of all joint owners to exploit, license or assign jointly owned patents. We did not receive consents from California or Vienna before entering into our license agreements with Dr. Emmanuelle Charpentier. Accordingly, unless and until we receive such consents, our license agreements may not be recognized in those countries requiring co-owner consent to a license. In countries where our license is not recognized, we may be subject to claims of patent infringement by California and/or Vienna to the extent that we are doing business in those countries or choose to do business there in the future. Even in countries that do not require co-owner consent to a license, we may be prohibited from exploiting the intellectual property, or we may be required to pay certain monies to California or Vienna to account for our exploitation of the intellectual property in those countries. As a result, in the absence of an agreement with California and Vienna, there may be countries in which we are unable to do business, or unable to do business on commercially reasonable terms, which could impact our commercialization plans and the willingness of strategic partners and other third parties to do business with us.

In the United States, each co-owner has the freedom to license and exploit the technology. As a result, we do not have exclusive access to any intellectual property rights that Dr. Emmanuelle Charpentier co-owns with California and Vienna. Our license with Dr. Charpentier is therefore non-exclusive. Furthermore, in the United States each co-owner may be required to be joined as a party to any claim or action we may wish to bring to enforce those patent rights. Moreover, in the United States, non-exclusive licenses have no standing to bring a patent infringement action before a court. Therefore, we have no ability to pursue third party infringement claims without cooperation of California and Vienna and potentially their licensees. Because we are unable to enforce our core patent rights licensed from Dr. Charpentier, we may be unable to prevent third parties from competing with us and may be unable to persuade companies to sublicense our technology, either of which could have a material adverse effect on our business.

If We Experience Disputes With The Third Parties That We In-license Intellectual Property Rights From, We Could Lose License Rights That Are Important To Our Business.

We license our foundational intellectual property from a third party, and we expect to continue to in-license additional third-party intellectual property rights as we expand our CRISPR/Cas9 gene-editing technology. Disputes may arise with the third parties from whom we license our intellectual property rights from for a variety of reasons, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships and obligations associated with sublicensing;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations, or may conflict in such a way that puts us in breach of one or more agreements, which would make us suspectible to lengthy and expensive disputes with one or more of our licensing partners. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations

under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

We May Not Be Successful In Obtaining Necessary Rights To Any Product Candidates We May Develop Through Acquisitions And In-licenses.

We currently have rights to intellectual property, through in-licenses from third parties, to identify and develop product candidates. Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us in the field of gene-editing technology and filing patent applications potentially relevant to our business. For example, we are aware of several third party patent applications that, if issued, may be construed to cover our CRISPR/Cas9 technology and product candidates. In order to avoid infringing these third party patents, we may find it necessary or prudent to obtain licenses from such third party intellectual property holders. We may also require licenses from third parties for certain modified or improved components of CRISPR/Cas9 technology, such as modified nucleic acids, as well as non-CRISPR/Cas9 technologies such as delivery methods that we are evaluating for use with product candidates we may develop. In addition, with respect to any patents we co-own with third parties, we may require licenses to such co-owners' interest to such patents. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for product candidates we may develop and CRISPR/Cas9 technology. The licensing or acquisition of third party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, or discontinue the practice of our core CRISPR/Cas9 gene-editing technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Issued Patents Covering Our Technology And Product Candidates Could Be Found Invalid Or Unenforceable If Challenged In Court.

If we or one of our licensors initiated legal proceedings against a third party to enforce a patent covering a product candidate we may develop or our technology, including CRISPR/Cas9, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties have raised challenges to the validity of certain of our in-licensed patent applications, such as our in-licensed CRISPR/Cas9 patent applications in the context of the U.S. interference proceedings and third party observations filed in Europe, and may in the future raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the loss of our patent applications or patents, or their narrowing in such a way that they no longer cover our technology or platform, or any product candidates that we may develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that

there is no invalidating prior art. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology or platform, or any product candidates that we may develop. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and prospects.

The Intellectual Property Landscape Around Gene-Editing Technology, Including CRISPR/Cas9, Is Highly Dynamic, And Third Parties May Initiate And Prevail In Legal Proceedings Alleging That We Are Infringing, Misappropriating, Or Otherwise Violating Their Intellectual Property Rights, The Outcome Of Which Would Be Uncertain And Could Have A Material Adverse Effect On The Success Of Our Business.

The field of gene editing, especially in the area of CRISPR/Cas9 technology, is still in its infancy, and no such products have reached the market. Due to the intense research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is in flux, and it may remain uncertain for the coming years. There may be significant intellectual property related litigation and proceedings, in addition to the ongoing interference proceedings, relating to our owned and in-licensed, and other third party, intellectual property and proprietary rights in the future.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market, and sell any product candidates that we may develop and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. We are subject to and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and any product candidates we may develop, including interference proceedings, post-grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the European Patent Office. Third parties, including parties involved in ongoing interference proceedings, may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. We are aware of certain third party patents and patent applications including, for example, the Broad patents involved in the current interference proceeding described above that may be asserted to encompass our CRISPR/Cas9 technology. If we are unable to prove that these patents are invalid and we are not able to obtain or maintain a license on commercially reasonable terms, such third parties could potentially assert infringement claims against us, which could have a material adverse effect on the conduct of our business. If we are found to infringe such third party patents, we and our partners may be required to pay damages, cease commercialization of the infringing technology, including our core CRISPR/Cas9 gene-editing technology, or obtain a license from such third parties, which may not be available on commercially reasonable terms or at all. Additionally we have not performed any freedom-to-operate analysis on specific product candidates at this stage to identify potential infringement risks. A proper analysis of that type will not be feasible until specific product candidates are designed.

Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, ownership, or priority. A court of competent jurisdiction could hold that these third party patents are valid, enforceable, and infringed, which could materially and adversely affect our ability to commercialize any product candidates we may develop and any other product candidates or technologies covered by the asserted third party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe a third party's intellectual property rights, and we are unsuccessful in demonstrating that such patents are invalid or unenforceable, we could be required to obtain a license from such third party to continue developing, manufacturing, and marketing any product candidates we may develop and our technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-

exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We also could be forced, including by court order, to cease developing, manufacturing, and commercializing the infringing technology or product candidates. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations, and prospects.

Intellectual Property Litigation Could Cause Us To Spend Substantial Resources And Distract Our Personnel From Their Normal Responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities and generally harm our business. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation in certain countries, including the United States, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing or misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Obtaining And Maintaining Our Patent Protection Depends On Compliance With Various Procedural, Document Submission, Fee Payment, And Other Requirements Imposed By Government Patent Agencies And Our Patent Protection Could Be Reduced Or Eliminated For Non-compliance With These Requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned or licensed patents and applications. In certain circumstances, we rely on our licensing partners to pay these fees due to U.S. and non-U.S. patent agencies. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. We are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, we may not be able to stop a competitor from marketing drugs that are the same as or similar to our product candidates, which would have a material adverse effect on our business.

Some Intellectual Property Which We Have In-licensed May Have Been Discovered Through Government Funded Programs And Thus May Be Subject To Federal Regulations Such As "march-in" Rights, Certain Reporting Requirements And A Preference For U.S.-based Manufacturers. Compliance With Such Regulations May Limit Our Exclusive Rights, And Limit Our Ability To Contract With Non-U.S. Manufacturers.

The intellectual property rights to which we have in-licensed under Dr. Emmanuelle Charpentier's joint interest are co-owned by California, which has indicated that the invention was made under Grant No. GM081879 awarded by the National Institute of Health. These rights are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations, also referred to as "march-in rights." The U.S. government also has the right to take title to these inventions if we, or the applicable contractor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable contractor to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

We May Not Be Able To Protect Our Intellectual Property And Proprietary Rights Throughout The World.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, the patent laws of some foreign countries do not afford intellectual property protection to the same extent as the laws of the United States. For example, unlike patent law in the United States, the patent law in Europe and many other jurisdictions precludes the patentability of methods of treatment of the human body and imposes substantial restrictions on the scope of claims it will grant if broader than specifically disclosed embodiments.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology

products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Changes To The Patent Law In The United States And Other Jurisdictions Could Diminish The Value Of Patents In General, Thereby Impairing Our Ability To Protect Our Product Candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a “first to file” system. The first-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could harm our business, results of operations and financial condition.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. For example, in *Association for Molecular Pathology v. Myriad Genetics, Inc*., the Supreme Court ruled that a “naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated,” and invalidated Myriad Genetics’s claims on the isolated BRCA1 and BRCA2 genes. Certain claims of our patents relate to CRISPR/Cas9 gene-editing technology as well as guide components that are directed to naturally occurring DNA sequences. To the extent that such claims are deemed to be directed to natural products, or to lack an inventive concept above and beyond an isolated natural product, a court may decide the claims are invalid under *Myriad*. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Europe’s planned

Unified Patent Court, scheduled to begin in 2017, may particularly present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. While that new court is being implemented to provide more certainty and efficiency to patent enforcement throughout Europe, it will also provide our competitors with a new forum to use to centrally revoke our European patents. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by that court. We will have the right to opt our patents out of that system over the first seven years of the court, but doing so may preclude us from realizing the benefits of the new unified court.

If We Are Unable To Protect The Confidentiality Of Our Trade Secrets, Our Business And Competitive Position Would Be Harmed.

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information and to maintain our competitive position. Trade secrets and know-how can be difficult to protect. In particular, we anticipate that with respect to our technology platform, these trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel from academic to industry scientific positions.

We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

If We Do Not Obtain Patent Term Extension And Data Exclusivity For Any Product Candidates We May Develop, Our Business May Be Materially Harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or term of any such extension is less than we request, we will be unable to rely on our patent position to forestall the marketing of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

Intellectual Property Rights Do Not Necessarily Address All Potential Threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make gene therapy products that are similar to any product candidates we may develop or utilize similar gene therapy technology but that are not covered by the claims of the patents that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending licensed patent applications or those that we may own in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We May Be Subject To Claims That Our Employees, Consultants, Or Advisors Have Wrongfully Used Or Disclosed Alleged Trade Secrets Of Their Current Or Former Employers Or Claims Asserting Ownership Of What We Regard As Our Own Intellectual Property.

Many of our employees, consultants, and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-

executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to This Offering and Ownership of Our Common Shares

If You Purchase Our Common Shares In This Offering, You Will Incur Immediate And Substantial Dilution In The Book Value Of Your Shares.

You will suffer immediate and substantial dilution in the net tangible book value of our common shares you purchase in this offering. Assuming an initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, after giving effect to this offering and the concurrent private placement, purchasers of common shares in this offering will experience immediate dilution of $ per share in net tangible book value of our common shares. In addition, after giving effect to this offering and the concurrent private placement, investors purchasing common shares in this offering will contribute % of the total amount invested by shareholders since inception but will only own % of the common shares outstanding. In the past, we issued options and other securities to acquire common shares at prices significantly below the initial public offering price. To the extent these outstanding securities are ultimately exercised, investors purchasing common shares in this offering will sustain further dilution. See “Dilution” for a more detailed description of the dilution to new investors in the offering.

We Have Broad Discretion In How We Use The Proceeds Of This Offering And The Concurrent Private Placement And May Not Use These Proceeds Effectively, Which Could Affect Our Results Of Operations And Cause Our Common Share Price To Decline.

We will have considerable discretion in the application of the net proceeds of this offering and the concurrent private placement. We anticipate that we will use the net proceeds from this offering to advance the development of our hemoglobinpathy programs and to progress additional pipeline candidates and to further optimize our CRISPR/Cas9 gene editing platform and delivery technologies as well as for manufacturing, working capital and general corporate purposes, which may include funding for the hiring of additional personnel, capital expenditures and the costs of operating as a public company. As a result, investors will be relying upon management’s judgment with only limited information about our specific intentions for the use of the balance of the net proceeds of this offering and the concurrent private placement. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our shareholders. In addition, pending their use, we may invest the net proceeds from this offering and the concurrent private placement in a manner that does not produce income or that loses value.

We Will Incur Increased Costs As A Result Of Operating As A Public Company And Our Management Will Be Required To Devote Substantial Time To New Compliance Initiatives And Corporate Governance Practices.

As a public company, and particularly after we are no longer an “emerging growth company,” we will incur significant legal, accounting and other expenses that we did not incur as a private company. SOX, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Market, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We expect that we will need to hire additional accounting, finance, and other personnel in connection with our becoming, and our efforts to comply with the requirements of being, a public company, and our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements will increase our legal and financial compliance costs

and will make some activities more time-consuming and costly. For example, we expect that the rules and regulations applicable to us as a public company may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. Furthermore, in anticipation of becoming a public company, we will need to adopt additional internal controls and disclosure controls and procedures and bear all of the internal and external costs of preparing and distributing periodic public reports in compliance with our obligation under the securities laws. We are currently evaluating these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to SOX Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants, adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by SOX Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

The Market Price Of Our Common Shares May Be Volatile And Fluctuate Substantially, Which Could Result In Substantial Losses For Investors Purchasing Shares In This Offering.

The initial public offering price for our common shares will be determined through negotiations with the underwriters. This initial public offering price may vary from the market price of our common shares after the offering. As a result, you may not be able to sell your common shares at or above the initial public offering price. Some of the factors that may cause the market price of our common shares to fluctuate include:

- the success of existing or new competitive products or technologies;
- the timing and results of any product candidates that we may develop;
- commencement or termination of collaborations for our product development and research programs;
- failure or discontinuation of any of our product development and research programs;
- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- developments or changing views regarding the use of genomic products, including those that involve gene editing;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs, or product candidates that we may develop;

- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common shares by us, our insiders, or other shareholders;
- expiration of market stand-off or lock-up agreement;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our common shares;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Broad market and industry factors may seriously affect the market price of our common shares, regardless of our actual operating performance. These fluctuations may be even more pronounced in the trading market for our common shares shortly following this offering. Following periods of such volatility in the market price of a company's securities, securities class action litigation has often been brought against that company. Because of the potential volatility of our common share price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management's attention and resources from our business.

An Active Trading Market For Our Common Shares May Not Develop And You May Not Be Able To Resell Your Shares At Or Above The Initial Public Offering Price.

Prior to this offering, there has been no public market for shares of our common shares. Although we anticipate that our common shares will be approved for listing on NASDAQ, an active trading market for our shares may never develop or be sustained following this offering. The initial public offering price of our common shares will be determined through negotiations between us and the underwriters. This initial public offering price may not be indicative of the market price of our common shares after this offering. If a market for our common shares does not develop or is not sustained, it may be difficult for you to sell your common shares at an attractive price or at all. We cannot predict the prices at which our common shares will trade. It is possible that in one or more future periods our results of operations may be below the expectations of public market analysts and investors, and, as a result of these and other factors, the price of our common shares may fall.

If Securities Analysts Do Not Publish Research Or Reports About Our Business Or If They Publish Negative Evaluations Of Our Common Shares, The Price Of Our Common Shares Could Decline.

The trading market for our common shares will rely in part on the research and reports that industry or financial analysts publish about us or our business. We may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our common shares would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our common shares, the price of our common shares could decline. If one or more of these analysts cease to cover our common shares, we could lose visibility in the market for our common shares, which in turn could cause our common share price to decline.

Sales Of A Substantial Number Of Our Common Shares In The Public Market Could Cause Our Share Price To Fall.

If our existing shareholders sell, or indicate an intention to sell, substantial amounts of our common shares in the public market after the lock-up and other legal restrictions on resale discussed in this prospectus lapse, the market price of our common shares could decline. Based upon the number of common shares, on an as-converted basis, outstanding as of December 31, 2015, upon the completion of this offering and the concurrent private placement, we will have outstanding a total of common shares, assuming no exercise of the underwriters' option to purchase an additional shares. Of these shares, as of the date of this prospectus, approximately common shares, plus any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable, without restriction, in the public market immediately following this offering, assuming that current shareholders do not purchase shares in this offering. The representatives of the underwriters, however, may, in their sole discretion, permit our officers, directors and other shareholders who are subject to these lock-up agreements to sell shares prior to the expiration of the lock-up agreements.

The lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus. After the lock-up agreements expire, based upon the number of common shares, on an as-converted basis, outstanding as of December 31, 2015, up to an additional common shares will be eligible for sale in the public market, approximately % of which shares are held by directors, executive officers and other affiliates and will be subject to certain limitations of Rule 144 under the Securities Act of 1933, as amended, or the Securities Act.

Upon completion of this offering and the concurrent private placement, common shares that are either subject to outstanding options, reserved for future issuance under our equity incentive plans or subject to outstanding warrants will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. If these additional common shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common shares could decline.

After this offering and the concurrent private placement, the holders of approximately common shares will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up agreements described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these shareholders could have a material adverse effect on the market our common shares.

We Are An "Emerging Growth Company," And The Reduced Disclosure Requirements Applicable To Emerging Growth Companies May Make Our Common Shares Less Attractive To Investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year in which we have total annual gross revenue of $1 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, which means the market value of our common shares that is held by non-affiliates exceeds $700 million as of the prior June 30th. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of SOX;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;

- being permitted to present only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this prospectus;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting burdens in this prospectus. In particular, we have provided only two years of audited financial statements and have not included all of the executive compensation information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common shares less attractive if we rely on these exemptions. If some investors find our common shares less attractive as a result, there may be a less active trading market for our common shares and our common share price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Our Executive Officers, Directors, Principal Shareholders And Their Affiliates Will Continue To Exercise Significant Influence Over Our Company After This Offering, Which Will Limit Your Ability To Influence Corporate Matters And Could Delay Or Prevent A Change In Corporate Control.

Certain principal shareholders and their affiliated entities as well as members of our executive team and board of directors own approximately , or approximately % after giving effect to this offering and the concurrent private placement, of our common shares. Depending on the level of attendance at our general meetings of shareholders, these shareholders may be in a position to determine the outcome of decisions taken at any such general meeting. Any shareholder or group of shareholders controlling more than 50% of the shares represented at our general meetings of shareholders may control any shareholder resolution requiring an absolute majority of the shares represented, including the election of members to the board of directors of our Company, certain decisions relating to our capital structure, the approval of certain significant corporate transactions and certain amendments to our articles of association. To the extent that the interests of these shareholders may differ from the interests of our other shareholders, the latter may be disadvantaged by any action that these shareholders may seek to pursue. Among other consequences, this concentration of ownership may have the effect of delaying or preventing a change in control and might therefore negatively affect the market price of our common shares.

See "Principal Shareholders" in this prospectus for more information regarding the ownership of our outstanding common shares by our executive officers, directors, principal shareholders and their affiliates.

We Do Not Expect To Pay Dividends In The Foreseeable Future.

We have not paid any dividends since our incorporation. Even if future operations lead to significant levels of distributable profits, we currently intend that any earnings will be reinvested in our business and that dividends will not be paid until we have an established revenue stream to support continuing dividends. The proposal to pay future dividends to shareholders will in addition effectively be at the discretion of our board of directors and shareholders after taking into account various factors including our business prospects, cash requirements, financial performance and new product development. In addition, payment of future dividends is subject to certain limitations pursuant to Swiss law or by our articles of association. See "Description of Share Capital and

Articles of Association." Accordingly, investors cannot rely on dividend income from our common shares and any returns on an investment in our common shares will likely depend entirely upon any future appreciation in the price of our common shares. Dividends paid on our common shares are subject to Swiss federal withholding tax, except if paid out of reserves from capital contributions ("*Kapitaleinlagen*"). See "Taxation—Swiss Tax Considerations" for a summary of certain Swiss tax consequences regarding dividends distributed to holders of our common shares.

We Are A Swiss Corporation. The Rights Of Our Shareholders May Be Different From The Rights Of Shareholders In Companies Governed By The Laws Of U.S. Jurisdictions.

We are a Swiss corporation. Our corporate affairs are governed by our articles of association and by Swiss law. The rights of our shareholders and the responsibilities of members of our board of directors may be different from the rights and obligations of shareholders and directors of companies governed by the laws of U.S. jurisdictions. In the performance of its duties, our board of directors is required by Swiss law to consider the interests of our Company, our shareholders and our employees with due observation of the principles of reasonableness and fairness. It is possible that the board of directors will consider interests that are different from, or in addition to, your interests as a shareholder. Swiss corporate law limits the ability of our shareholders to challenge resolutions made or other actions taken by our board of directors in court. Our shareholders generally are not permitted to file a suit to reverse a decision or an action taken by our board of directors but are instead only permitted to seek damages for breaches of the duty of care and loyalty. As a matter of Swiss law, shareholder claims against a member of our board of directors for breach of the duty of care and loyalty would have to be brought in Basel, Switzerland, or where the relevant member of our board of directors is domiciled. In addition, under Swiss law, any claims by our shareholders against us must be brought exclusively in Basel, Switzerland. See "Description of Share Capital and Articles of Association" and "Comparison of Swiss Law and Delaware Law."

We Will Need A Shareholders' Resolution Regarding The Authorized Share Capital Increase, Which If Obtained, Could Be Blocked.

Prior to this offering, we will need to obtain a shareholder resolution for the increase in authorized share capital increase. Even if we get this approval, as with all share capital increases in Switzerland, the registration of the capital increase in the commercial register of the Canton of Basel-Stadt may be blocked by a shareholder and the underlying shareholders' resolution may be challenged within two months after such shareholders' meeting and, therefore, prevent or delay the completion of this offering.

Our Common Shares Are Issued Under The Laws Of Switzerland, Which May Not Protect Investors In A Similar Fashion Afforded By Incorporation In A U.S. State.

We are organized under the laws of Switzerland. A further summary of applicable Swiss company law is contained in this prospectus under "Description of Share Capital and Articles of Association" and "Comparison of Swiss Law and Delaware Law." However, there can be no assurance that Swiss law will not change in the future or that it will serve to protect investors in a similar fashion afforded under corporate law principles in the U.S., which could adversely affect the rights of investors.

Our Status As A Swiss Corporation May Limit Our Flexibility With Respect To Certain Aspects Of Capital Management And May Cause Us To Be Unable To Make Distributions Without Subjecting Our Shareholders To Swiss Withholding Tax.

Swiss law allows our shareholders to authorize share capital that can be issued by the board of directors without additional shareholder approval. This authorization is limited to 50% of the existing registered share capital and must be renewed by the shareholders every two years. Additionally, subject to specified exceptions, Swiss law grants preemptive rights to existing shareholders to subscribe to any new issuance of shares. Swiss law also does not provide as much flexibility in the various terms that can attach to different classes of shares as the laws of some

other jurisdictions. Swiss law also reserves for approval by shareholders certain corporate actions over which a board of directors would have authority in some other jurisdictions. For example, dividends must be approved by shareholders. These Swiss law requirements relating to our capital management may limit our flexibility, and situations may arise where greater flexibility would have provided substantial benefits to our shareholders.

Under Swiss law, a Swiss corporation may pay dividends only if the corporation has sufficient distributable profits from previous fiscal years, or if the corporation has distributable reserves, each as evidenced by its audited statutory balance sheet, and after allocations to reserves required by Swiss law and our articles of association have been deducted. Freely distributable reserves are generally booked either as "free reserves" or as "capital contributions" (*Kapitaleinlagen*, contributions received from shareholders) in the "reserve from capital contributions." Distributions may be made out of registered share capital—the aggregate par value of a company's registered shares—only by way of a capital reduction. Upon completion of this offering, we expect the Company to have CHF of qualifying capital contributions and CHF of registered share capital on its audited statutory balance sheet. We expect the aggregate of these amounts (less the minimum registered share capital and legal reserve of together CHF 150,000) to represent the amount available for future dividends or capital reductions on a Swiss withholding tax-free basis. We will not be able to pay dividends or make other distributions to shareholders on a Swiss withholding tax-free basis in excess of that amount unless the Company increases its share capital or its reserves from capital contributions. We would also be able to pay dividends out of distributable profits or freely distributable reserves, but such dividends would be subject to Swiss withholding taxes. There can be no assurance that we will have sufficient distributable profits, free reserves, reserves from capital contributions or registered share capital to pay a dividend or effect a capital reduction, that our shareholders will approve dividends or capital reductions proposed by us or that we will be able to meet the other legal requirements for dividend payments or distributions as a result of capital reductions.

Generally, Swiss withholding tax of 35% is due on dividends and similar distributions to our shareholders, regardless of the place of residency of the shareholder, unless the distribution is made to shareholders out of (i) a reduction of par value or (ii) assuming certain conditions are met, qualifying capital contributions accumulated on or after January 1, 1997. A U.S. holder that qualifies for benefits under the Convention between the United States of America and the Swiss Confederation for the Avoidance of Double Taxation with Respect to Taxes on Income, or the U.S.-Swiss Treaty, may apply for a refund of the tax withheld in excess of the15% treaty rate (or in excess of the 5% reduced treaty rate for qualifying corporate shareholders with at least 10% participation in our voting shares, or for a full refund in the case of qualified pension funds). There can be no assurance that we will have sufficient qualifying capital contributions to pay dividends free from Swiss withholding tax, or that Swiss withholding rules will not be changed in the future. In addition, we cannot provide assurance that the current Swiss law with respect to distributions out of qualifying capital contributions will not be changed or that a change in Swiss law will not adversely affect us or our shareholders, in particular as a result of distributions out of qualifying capital contributions becoming subject to additional corporate law or other restrictions. There are currently motions pending in the Swiss Parliament that may limit the distribution of qualifying capital contributions. In addition, over the long term, the amount of par value available to us for par value reductions or qualifying capital contributions available to us to pay out as distributions is limited. If we are unable to make a distribution through a reduction in par value or out of qualifying capital contributions, we may not be able to make distributions without subjecting our shareholders to Swiss withholding taxes.

Under present Swiss tax laws, repurchases of shares for the purposes of cancellation are treated as a partial liquidation subject to 35% Swiss withholding tax on the difference between the repurchase price and the par value except, since January 1, 2011, to the extent attributable to qualifying capital contributions (*Kapitaleinlagen*) if any, and to the extent that, the repurchase of shares is out of retained earnings or other taxable reserves, the Swiss withholding becomes due. No partial liquidation treatment applies and no withholding tax is triggered if the shares are not repurchased for cancellation but held by the Company as treasury shares. However, should the Company not resell such treasury shares within six years, the withholding tax becomes due at the end of the six year period.

You May Be Subject To Adverse U.S. Federal Income Tax Consequences If We Are Classified As A Controlled Foreign Corporation.

Each "Ten Percent Shareholder" (as defined below) in a non-U.S. corporation that is classified as a "controlled foreign corporation," or a CFC, for United States federal income tax purposes generally is required to include in income for U.S. federal tax purposes such Ten Percent Shareholder's pro rata share of the CFC's "Subpart F income" and investment of earnings in U.S. property, even if the CFC has made no distributions to its shareholders. Subpart F income generally includes dividends, interest, rents and royalties, gains from the sale of securities and income from certain transactions with related parties. In addition, a Ten Percent Shareholder that realizes gain from the sale or exchange of shares in a CFC may be required to classify a portion of such gain as dividend income rather than capital gain. A non-U.S. corporation generally will be classified as a CFC for United States federal income tax purposes if Ten Percent Shareholders own, directly or indirectly, more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A "Ten Percent Shareholder" is a United States person (as defined by the U.S. Internal Revenue Code of 1986, as amended (the "Code")) who owns or is considered to own 10% or more of the total combined voting power of all classes of stock entitled to vote of such corporation. The determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain.

We believe that we were a CFC for the taxable year ended December 31, 2015 and that we were likely a CFC prior to this offering in the current taxable year, and thus will likely be a CFC for the current taxable year. However, the Company's analysis with respect to its status as a CFC for the current tax year is still ongoing. Additionally, it is possible that, following this offering, a shareholder treated as a U.S. person for U.S. federal income tax purposes will acquire, directly or indirectly, enough shares to be treated as a Ten Percent Shareholder and, together with any other Ten Percent Shareholders, cause the Company to be treated as a CFC for a taxable year following the year of this offering. U.S. holders should consult their own tax advisors with respect to the potential adverse U.S. tax consequences of becoming a Ten Percent Shareholder in a CFC. If we are classified as both a CFC and a PFIC, we generally will not be treated as a PFIC with respect to those U.S. holders that meet the definition of a Ten Percent Shareholder during the period in which we are a CFC.

Our U.S. Shareholders May Suffer Adverse Tax Consequences If We Are Characterized As A Passive Foreign Investment Company.

Generally, if, for any taxable year, at least 75% of our gross income is passive income, or at least 50% of the value of our assets is attributable to assets that produce passive income or are held for the production of passive income, including cash, we would be characterized as a passive foreign investment company, or PFIC, for U.S. federal income tax purposes. For purposes of these tests, passive income includes dividends, interest, and gains from the sale or exchange of investment property and rents and royalties other than rents and royalties which are received from unrelated parties in connection with the active conduct of a trade or business. If we are characterized as a PFIC, U.S. holders of our common shares may suffer adverse tax consequences, including having gains realized on the sale of the common shares treated as ordinary income, rather than capital gain, the loss of the preferential rate applicable to dividends received on the common shares by individuals who are U.S. holders, and having interest charges apply to distributions by us and the proceeds of sales of the common shares. See "Material U.S. Federal Income Tax Considerations to U.S. Holders—Passive Foreign Investment Company Considerations."

Our status as a PFIC will depend on the composition of our income and the composition and value of our assets (which, assuming we were a non-publicly traded CFC for the year being tested for purposes of the PFIC rules, must be measured by the adjusted tax basis of our assets or, if we were a publicly traded CFC or not a CFC for such year, the total value of our assets may be determined in part by reference to the quarterly market value of our common shares, which may be volatile) from time to time. Our status may also depend, in part, on how, and how quickly, we utilize the cash proceeds from the global offering in our business. Based on our belief that we were a CFC for the 2015 taxable year and that we were likely a CFC prior to this offering in the current taxable

year (and thus are required to determine our PFIC Status under the asset test by reference to the adjusted tax basis of our assets) and on certain estimates of our gross assets, our intended use of proceeds of this offering, and the nature of our business, we believe we were a PFIC for the 2015 taxable year and will likely be a PFIC with respect to the 2016 taxable year. However, the Company's analysis with respect to its status as a PFIC for the current taxable year is still ongoing. Because the total value of our assets may be measured in part by the market value of our common shares in 2017, we expect that we should not be classified as a PFIC for the taxable year ending December 31, 2017. However, our status as a PFIC is a fact-intensive determination made on an annual basis and we cannot provide any assurances regarding our PFIC status for any past, current or future taxable years. We do not currently intend to provide the information necessary for U.S. holders to make a "qualified electing fund," or QEF, election if we are treated as a PFIC for any taxable year, and prospective investors should assume that a QEF election will not be available.

U.S. Shareholders May Not Be Able To Obtain Judgments Or Enforce Civil Liabilities Against Us Or Our Executive Officers Or Members Of Our Board Of Directors.

We are organized under the laws of Switzerland and our registered office and domicile is located in Basel, Switzerland. Moreover, certain of our directors and executive officers and a number of directors of each of our subsidiaries are not residents of the United States, and all or a substantial portion of the assets of such persons are located outside the United States. As a result, it may not be possible for investors to effect service of process within the United States upon us or upon such persons or to enforce against them judgments obtained in U.S. courts, including judgments in actions predicated upon the civil liability provisions of the federal securities laws of the United States. We have been advised by our Swiss counsel that there is doubt as to the enforceability in Switzerland of original actions, or in actions for enforcement of judgments of U.S. courts, of civil liabilities to the extent solely predicated upon the federal and state securities laws of the United States. Original actions against persons in Switzerland based solely upon the U.S. federal or state securities laws are governed, among other things, by the principles set forth in the Swiss Federal Act on Private International Law. This statute provides that the application of provisions of non-Swiss law by the courts in Switzerland shall be precluded if the result is incompatible with Swiss public policy. Also, mandatory provisions of Swiss law may be applicable regardless of any other law that would otherwise apply.

Switzerland and the United States do not have a treaty providing for reciprocal recognition and enforcement of judgments in civil and commercial matters. The recognition and enforcement of a judgment of the courts of the United States in Switzerland is governed by the principles set forth in the Swiss Federal Act on Private International Law. This statute provides in principle that a judgment rendered by a non-Swiss court may be enforced in Switzerland only if:

- the non-Swiss court had jurisdiction pursuant to the Swiss Federal Act on Private International Law;
- the judgment of such non-Swiss court has become final and non-appealable;
- the judgment does not contravene Swiss public policy;
- the court procedures and the service of documents leading to the judgment were in accordance with the due process of law; and
- no proceeding involving the same position and the same subject matter was first brought in Switzerland, or adjudicated in Switzerland, or was earlier adjudicated in a third state and this decision is recognizable in Switzerland.

Our Status As A Swiss Corporation Means That Our Shareholders Enjoy Certain Rights That May Limit Our Flexibility To Raise Capital, Issue Dividends And Otherwise Manage Ongoing Capital Needs.

Swiss law reserves for approval by shareholders certain corporate actions over which a board of directors would have authority in some other jurisdictions. For example, the payment of dividends and cancellation of

treasury shares must be approved by shareholders. Swiss law also requires that our shareholders themselves resolve to, or authorize our board of directors to, increase our share capital. While our shareholders may authorize share capital that can be issued by our board of directors without additional shareholder approval, Swiss law limits this authorization to 50% of the issued share capital at the time of the authorization. The authorization, furthermore, has a limited duration of up to two years and must be renewed by the shareholders from time to time thereafter in order to be available for raising capital. Additionally, subject to specified exceptions, including exceptions explicitly described in our articles of association, Swiss law grants pre-emptive rights to existing shareholders to subscribe for new issuances of shares. Swiss law also does not provide as much flexibility in the various rights and regulations that can attach to different categories of shares as do the laws of some other jurisdictions, such as in the United States. These Swiss law requirements relating to our capital management may limit our flexibility, and situations may arise where greater flexibility would have provided benefits to our shareholders. See “Description of Share Capital and Articles of Association” and “Comparison of Swiss Law and Delaware Law.”

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains statements that constitute forward-looking statements. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, product candidates, product pipeline, and planned preclinical and clinical studies, regulatory approvals, research and development costs, timing and likelihood of success, as well as plans and objectives of management for future operations are forward-looking statements. Many of the forward-looking statements contained in this prospectus can be identified by the use of forward-looking words such as “anticipate,” “believe,” “could,” “expect,” “should,” “plan,” “intend,” “estimate,” “will” and “potential,” among others.

Forward-looking statements appear in a number of places in this prospectus and include, but are not limited to, statements regarding our plans, intent, belief or current expectations. Forward-looking statements are based on our management’s beliefs and assumptions and on information currently available to our management. Such statements are subject to risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including, but not limited to, those identified under the section entitled “Risk Factors” in this prospectus. These risks and uncertainties include factors relating to:

- the initiation, cost, timing, progress and results of our research and development activities, preclinical studies and future clinical trials;
- our ability to create a pipeline of product candidates;
- our ability to advance any product candidate into, and successfully complete clinical trials;
- our ability to obtain and maintain regulatory approval of our future product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations;
- our plans to research, develop and commercialize our future product candidates;
- the success of our joint venture with Bayer HealthCare LLC and our collaboration with Vertex Pharmaceuticals, Incorporated;
- our ability to obtain and maintain intellectual property protection for our future product candidates;
- the size and growth potential of the markets for our future product candidates, and our ability to serve those markets;
- our ability to successfully commercialize our current and future product candidates;
- the rate and degree of market acceptance of our current and future product candidates;
- regulatory developments in the United States and foreign countries;
- developments relating to gene-editing technologies including CRISPR/Cas9;
- the success of competing therapies that are or become available;
- our ability to retain key scientific or management personnel;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our use of the proceeds from this offering and the concurrent private placement; and
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and need for additional financing.

We caution you that the foregoing list may not contain all of the forward-looking statements made in this prospectus.

You should not rely upon forward-looking statements as predictions of future events. We have based the forward-looking statements contained in this prospectus primarily on our current expectations and projections about future events and trends that we believe may affect our business, financial condition, results of operations

and prospects. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions described under the sections in this prospectus entitled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risks and uncertainties may emerge from time to time, and it is impossible for management to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. The forward-looking statements contained in this prospectus are excluded from the safe harbor protection provided by the Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act.

MARKET AND INDUSTRY DATA

This prospectus contains industry, market and competitive position data that are based on industry publications and studies conducted by third parties as well as our own internal estimates and research. These industry publications and third-party studies generally state that the information that they contain has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe that each of these publications, third-party studies and our internal research is reliable and that the definition of our market and industry is appropriate, you are cautioned not to give undue weight to this information.

USE OF PROCEEDS

We estimate that the net proceeds from the sale of common shares in this offering, excluding the concurrent private placement, will be approximately $ million at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the underwriting discount and estimated offering expenses payable by us. If the underwriters exercise their over-allotment option in full, we estimate that the net proceeds will be approximately $ million, after deducting the underwriting discount and estimated offering expenses payable by us.

Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) our net proceeds by $ million, assuming the number of shares offered by us, as set forth on the cover of this prospectus, remains the same and after deducting the underwriting discount and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase (decrease) of 1,000,000 in the number of shares we are offering would increase (decrease) the net proceeds to us from this offering, after deducting the underwriting discount and estimated offering expenses payable by us, by approximately $ million, assuming the assumed initial public offering price stays the same.

Bayer Global Investments B.V. has agreed to purchase from us concurrently with this offering in a private placement up to $35 million of our common shares at a price per share equal to the initial public offering price. See “Concurrent Private Placement.”

We are undertaking this offering in order to access the public capital markets, to increase our liquidity and to support continued development of our research programs. We intend to use the net proceeds of this offering and the concurrent private placement, together with our existing cash and cash equivalents, as follows:

- approximately $ million to advance the development of our hemoglobinopathy programs;
- approximately $ million to progress additional pipeline candidates;
- approximately $ to further optimize our CRISPR/Cas9 gene editing platform and develop delivery technologies; and
- the remainder for manufacturing, working capital and general corporate purposes.

However, due to the uncertainties inherent in the product development process, it is difficult to estimate with certainty the exact amounts of the net proceeds from this offering and the concurrent private placement that may be used for the above purposes. The amount and timing of our actual expenditures will depend upon numerous factors, including the results of our research and development efforts, the timing and success of our ongoing preclinical studies or preclinical studies we may commence in the future and the timing of regulatory submissions. As a result, our management will have broad discretion over the use of the net proceeds from this offering and the concurrent private placement, and investors will be relying on our judgment regarding the application of the net proceeds. In addition, we might decide to postpone or not pursue certain preclinical activities if the net proceeds from this offering and the concurrent private placement and our other sources of cash are less than expected.

Although it is difficult to predict future liquidity requirements, we believe that the net proceeds from this offering and the concurrent private placement, along with our existing cash and cash equivalents, together with interest thereon, will be sufficient to fund our operations for at least the next 24 months.

We believe opportunities may exist from time to time to expand our current business through acquisitions or in-licenses of complementary companies or technologies. While we have no current agreements, commitments or understandings for any specific acquisitions or in-licenses at this time, we may use a portion of the net proceeds for these purposes.

Pending the use of the proceeds from this offering and the concurrent private placement, we intend to invest the net proceeds in interest-bearing, investment-grade securities, certificates of deposit or direct or guaranteed obligations of the U.S. and Swiss governments.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

Under Swiss law, any dividend must be proposed by our board of directors and approved by our shareholders. In addition, our auditors must confirm that the dividend proposal of our board of directors conforms to Swiss statutory law and our articles of association. A Swiss corporation may pay dividends only if it has sufficient distributable profits brought forward from the previous business years ("*Gewinnvortrag*") or if it has distributable reserves ("*freie Reserven*"), each as evidenced by its audited standalone statutory balance sheet prepared pursuant to Swiss law and after allocations to reserves required by Swiss law and its articles of association have been deducted. Distributable reserves are generally booked either as "free reserves" ("*freie Reserven*") or as "reserve from capital contributions" *("Kapitaleinlagereserven")*. Distributions out of issued share capital, which is the aggregate nominal value of a corporation's issued shares, may be made only by way of a share capital reduction. See "Description of Share Capital and Articles of Association."

CAPITALIZATION

The following table sets forth our cash and total capitalization as of December 31, 2015 on:

- an actual basis;
- a pro forma basis to give effect to:
  - (i) the conversion of all 5,651,105 of our outstanding preferred shares into common shares on a one-for-one basis immediately prior to the closing of this offering;
  - (ii) the issuance of 98,405 common shares to Dr. Emmanuelle Charpentier immediately prior to the closing of this offering pursuant to the Call Option Agreement;
  - (iii) the conversion of the convertible loan, including accrued interest, issued in October 2015 into 1,233,296 Series B Preferred Shares, and then converted into common shares on a one-for-one basis immediately prior to the closing of this offering; and
  - (iv) the filing and effectiveness of our amended and restated articles of association and creation of authorized and conditional share capital of common shares upon closing of this offering; and
- a pro forma as adjusted basis to further reflect:
  - (i) the receipt of the estimated net proceeds from the sale of common shares in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the underwriting discount and estimated expenses payable by us; and
  - (ii) the issuance and sale by us in the concurrent private placement of common shares to Bayer Global Investments B.V., assuming an initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus.

The pro forma as adjusted information below is illustrative only, and our capitalization following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this table in conjunction with “Use of Proceeds,” “Selected Consolidated Financial and Other Information” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our audited consolidated financial statements and related notes included elsewhere in this prospectus.

	As of December 31, 2015		
	Actual	Pro Forma	Pro Forma As Adjusted (1)
	(in thousands, except share and per share data)		
Cash	$ 155,961	$ 155,961	
Convertible loan, including accrued interest of $97 as of December 31, 2015 and $0 pro forma	38,336	—	
Redeemable convertible preferred shares (Series A-1, Series A-2, Series A-3, Series B), CHF 0.10 par value; 5,651,105 shares authorized, issued, and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	64,521	—	
Shareholders’ (deficit) equity:			
Common shares, CHF 0.10 par value; 1,658,428 shares authorized, issued, and outstanding, actual; 8,641,234 shares authorized, issued, and outstanding, pro forma; shares authorized, shares issued and outstanding, pro forma as adjusted	181	879	
Additional paid-in capital	4,636	106,971	
Accumulated deficit	(33,906)	(34,110)	
Total shareholders’ (deficit) equity	(29,124)	73,733	
Total capitalization	73,733	73,733	

(1) A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) each of pro forma as adjusted cash and cash equivalents, additional paid-in capital, total capitalization and total shareholders' equity by $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the underwriting discount and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase (decrease) of 1,000,000 in the number of shares offered by us would increase (decrease) pro forma as adjusted cash and cash equivalents, additional paid-in capital, total shareholders' equity and capitalization by $ million, assuming an initial public offering price of $ per share, after deducting the underwriting discount and estimated offering expenses payable by us.

The number of common shares in the table above excludes:

- 581,999 of our common shares issuable upon the exercise of options outstanding under our 2015 Stock Option Plan as of December 31, 2015 at an exercise price of $10.44 per common share;
- 42,838 unvested restricted stock share awards granted under our 2015 Stock Option Plan;
- of our common shares reserved for future issuance under our 2016 Stock Option Plan, which will become effective immediately prior to the completion of this offering; and
- common shares reserved for issuance under our 2016 Employee Stock Purchase Plan, or ESPP, which will become effective immediately prior to the completion of this offering.

DILUTION

If you invest in our common shares, your interest will be diluted to the extent of the difference between the initial public offering price per share and the pro forma as adjusted net tangible book value per share of our common shares immediately after this offering.

Net tangible book value is determined by dividing our total tangible assets less our total liabilities by the number of our common shares outstanding. Our historical net tangible book value as of December 31, 2015 was $34.9 million, or $21.07, per common share. Our pro forma net tangible book value as of December 31, 2015, before giving effect to this offering and the concurrent private placement, was $ million, or $ per common share, based on the total number of our common shares outstanding as of December 31, 2015, after giving effect to (i) the conversion of all 5,651,105 of our preferred shares outstanding as of December 31, 2015 into common shares on a one-for-one basis immediately prior to the closing of this offering, (ii) the issuance of 98,405 common shares to Dr. Emmanuelle Charpentier immediately prior to the closing of this offering pursuant to the Call Option Agreement, and (iii) the conversion of the convertible loan, including accrued interest, issued in October 2015 into 1,233,296 Series B Preferred Shares, and then into common shares on a one-for-one basis immediately prior to the closing of this offering.

Dilution per share to new investors represents the difference between the amount per share paid by purchasers of common shares in this offering and the pro forma as adjusted net tangible book value per common share immediately after completion of this offering and the concurrent private placement. After giving effect to our sale of common shares in this offering and common shares in the concurrent private placement, both at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the underwriting discounts and estimated expenses payable by us. Our pro forma as adjusted net tangible book value as of December 31, 2015 would have been $ million, or $ per share. This represents an immediate increase in as adjusted net tangible book value of $ per share to existing shareholders and an immediate dilution of $ per share to investors participating in this offering, as illustrated in the following table:

Assumed initial public offering price per share		$
Historical net tangible book value per share at December 31, 2015	$ 21.07	
Increase per share attributable to pro forma adjustments		
Pro forma net tangible book value per share at December 31, 2015		
Increase in pro forma net tangible book attributable to this offering and the concurrent private placement		
Pro forma as adjusted net tangible book value per share after this offering and the concurrent private placement		
Dilution per share to investors participating in this offering		$

Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) our as pro forma as adjusted net tangible book value by approximately $ million, or approximately $ per share, and the dilution per share to investors in this offering by approximately $ per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the underwriting discount and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase (decrease) of 1,000,000 shares in the number of shares offered by us would increase (decrease) our pro forma as adjusted net tangible book value by approximately $ million, or approximately $ per share, and decrease the pro forma dilution per share to investors in this offering by approximately $ per share, assuming an initial public offering price of $ per share, after deducting the underwriting discount and estimated offering expenses payable by us. The pro forma as adjusted information discussed above is illustrative only and will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing.

If the underwriters' over-allotment option is exercised in full, the pro forma as adjusted net tangible book value per share after this offering would be $ per share, the increase in pro forma as adjusted net tangible book value per share to existing shareholders would be $ per share and the dilution to new investors purchasing shares in this offering would be $ per share.

The following table shows, at December 31, 2015, on a pro forma as adjusted basis, after giving effect to the pro forma adjustments described above, the number of common shares purchased from us, the total consideration paid to us and the average price paid per share by existing shareholders and by new investors purchasing common shares in this offering and the concurrent private placement at an assumed initial public offering price of $ per share, before deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	Total Shares		Total Consideration		Average Price per Share
	Number	Percent	Amount	Percent	
Existing shareholders before this offering					
Concurrent private placement investor					
Investors participating in this offering					
Total		100.0%		100.0%	

Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share, would increase (decrease) the total consideration paid to us by new investors and total consideration paid to us by all shareholders by $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the underwriting discount and estimated offering expenses payable by us. An increase (decrease) of 1,000,000 shares in the number of shares offered by us would increase (decrease) the total consideration paid to us by new investors and total consideration paid to us by all shareholders by approximately $ million, assuming an initial public offering price of $ per share, after deducting the underwriting discount and estimated offering expenses payable by us.

The calculations above are based on (i) 7,309,533 shares outstanding as of December 31, 2015, and (ii) after giving effect to the pro forma transactions but exclude:

- 581,999 of our common shares issuable upon the exercise of options outstanding under our 2015 Stock Option Plan as of December 31, 2015 at an exercise price of $10.44 per common share;
- 42,838 unvested restricted share awards granted under our 2015 Stock Option Plan;
- of our common shares reserved for future issuance under our 2016 Stock Option Plan, which will become effective immediately prior to the completion of this offering; and
- common shares reserved for issuance under our 2016 Employee Stock Purchase Plan, or ESPP, which will become effective immediately prior to the completion of this offering.

To the extent that any outstanding options are exercised, new options are issued under our share-based compensation plans or we issue additional common shares in the future, there will be further dilution to investors participating in this offering.

EXCHANGE RATES

The following table sets forth, for the periods indicated, the high, low, average and period-end exchange rates for the purchase of U.S. dollars expressed in CHF per U.S. dollar. The average rate is calculated by using the average of the U.S. Federal Reserve Bank's reported exchange rates on each day during a monthly period and on the last day of each month during an annual period. On April 29, 2016, the exchange rate as reported by the U.S. Federal Reserve Bank was CHF .9598 to USD $1.00. In this prospectus, translations from CHF to U.S. dollars were made at the rate of 1.0017 to USD $1.00, the official exchange rate quoted as of December 31, 2015 by the U.S. Federal Reserve Bank.

	Period-end	Average for Period	Low	High
		(CHF per U.S. dollar)		
Years Ended December 31:				
2011	0.9374	0.8802	0.7296	0.9755
2012	0.9155	0.9331	0.8949	0.9957
2013	0.8904	0.9241	0.8856	0.9814
2014	0.9934	0.9195	0.8712	0.9934
2015	1.0017	0.9654	0.8488	1.0305
Months Ended:				
January 31, 2016	1.0226	1.0082	0.9972	1.0226
February 29, 2016	0.9960	0.9920	0.9706	1.0202
March 31, 2016	0.9583	0.9811	0.9583	0.9994
April 30, 2016	0.9598	0.9634	0.9537	0.9774
May 2016 (through May 6, 2016)	0.9697	0.9611	0.9541	0.9697

SELECTED CONSOLIDATED FINANCIAL DATA

The following tables summarize our consolidated financial data as of the dates and for the periods indicated. The financial data for the years ended December 31, 2015 and 2014 have been derived from our audited consolidated financial statements.

Our historical results are not necessarily indicative of the results that may be expected in the future. Our interim consolidated financial results for the periods presented are not necessarily indicative of results for a full year or for any subsequent interim period. The following selected financial data should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements included elsewhere in this prospectus.

	Year Ended December 31,	
	2014	2015
	(in thousands, except share and per share amounts)	
Statement of Operations Data:		
Collaboration revenue	$ —	$ 247
Operating expenses:		
Research and development	1,513	12,573
General and administrative	5,114	13,403
Total operating expenses	6,627	25,976
Operating loss	(6,627)	(25,729)
Other expense, net	(236)	(92)
Benefit from (provision for) income taxes	63	(7)
Net loss	(6,800)	(25,828)
Foreign currency translation adjustment	(2)	(6)
Comprehensive loss	$ (6,802)	$ (25,834)
Reconciliation of net loss to net loss attributable to common shareholders:		
Net loss	(6,800)	(25,828)
Loss attributable to noncontrolling interest	536	325
Loss on extinguishment of redeemable convertible preferred shares	(745)	—
Net loss attributable to common shareholders	(7,009)	(25,503)
Net loss per share attributable to common shareholders, basic and diluted	(6.56)	(16.88)
Weighted-average common shares outstanding, basic and diluted(1)	1,068,000	1,511,225
Pro-forma net loss per share, basic and diluted (unaudited)		(4.20)
Pro-forma weighted-average common shares outstanding, basic and diluted (unaudited)		6,072,412

(1) See Note 2 in the notes to our consolidated financial statements appearing at the end of this prospectus for a description of the method used to calculate basic and diluted net loss per share and pro forma basic and diluted net loss per share.

	As of December 31, 2015 Actual (in thousands)
Balance Sheet Data:	
Cash	$ 155,961
Working capital	146,685
Total assets	159,423
Redeemable convertible preferred shares	64,521
Total shareholders' (deficit) equity	(29,124)

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read together with our consolidated financial statements and related notes and other financial information appearing elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a leading gene editing company focused on the development of CRISPR/Cas9-based therapeutics. CRISPR/Cas9 is a revolutionary gene editing technology that allows for precise, directed changes to genomic DNA. The application of CRISPR/Cas9 for gene editing was co-invented by one of our scientific founders, Dr. Emmanuelle Charpentier, who, along with her collaborators, published work elucidating how CRISPR/Cas9, a naturally occurring viral defense mechanism found in bacteria, can be adapted for use in gene editing. We are applying this technology to potentially treat a broad set of rare and common diseases by disrupting, correcting or regulating the genes related to the disease. We believe that our scientific expertise, together with our approach, may enable an entirely new class of highly active and potentially curative treatments for patients for whom current biopharmaceutical approaches have had limited success.

We are pursuing a two-pronged product development strategy to our product development programs using both *ex vivo* and *in vivo* approaches. Our most advanced programs in hemoglobinopathies use an *ex vivo* approach, whereby cells are harvested from a patient, treated with a CRISPR/Cas9-based therapeutic and reintroduced into the patient. Beyond these lead programs, we are pursuing a number of additional *ex vivo* applications, as well as select *in vivo* applications whereby the CRISPR/Cas9 therapeutic is delivered directly to target cells within the human body. Our initial *in vivo* applications will leverage well-established delivery technologies for gene based therapeutics.

Since our inception in October 2013, we have devoted substantially all of our resources to initiating conducting our research and development efforts, identifying potential product candidates, undertaking drug discovery and preclinical development activities, building and protecting our intellectual property portfolio, organizing and staffing our company, business planning, raising capital, and providing general and administrative support for these operations. To date, we have primarily financed our operations through private placements of our preferred shares and convertible notes, and collaboration agreements with strategic partners. From our inception through December 31, 2015, we raised an aggregate of $177.5 million, of which $64.3 million consisted of gross proceeds from private placements of our preferred shares, $38.2 million from the issuance of convertible notes and $75.0 million from an upfront payment under our collaboration with Vertex Pharmaceuticals, Incorporated, or Vertex.

All of our revenue to date has been collaboration revenue. We have incurred significant net operating losses in every year since our inception and expect to continue to incur net operating losses for the foreseeable future. As of December 31, 2015, we had $156.0 million in cash and an accumulated deficit of $33.9 million. We expect to continue to incur significant expenses and increasing operating losses for the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase significantly as we continue our current research programs and development activities; seek to identify additional research programs and additional product candidates; initiate preclinical testing and clinical trials for any product candidates we identify and develop, maintain, expand and protect our intellectual property portfolio, including in the ongoing interference proceeding with respect to our in-licensed intellectual property; further develop our gene editing platform; hire additional research, clinical and scientific personnel; and incur additional costs associated with operating as a public company.

Collaboration Agreement and Joint Venture Agreement

In October 2015, we entered into a strategic research collaboration agreement with Vertex focused on the development of CRISPR/Cas9-based therapies. Under the terms of our agreement, we received an upfront, nonrefundable payment of $75.0 million and $30.0 million in convertible loan proceeds.

In December 2015, we entered into an agreement, the JV Agreement, with Bayer HealthCare LLC , or Bayer Healthcare, to create a joint venture, Casebia Therapeutics LLP, the JV, to discover, develop and commercialize new breakthrough therapeutics to cure blood disorders, blindness, and congenital heart disease. Under the agreement, Bayer Healthcare will make available its protein engineering expertise and relevant disease know-how and we will contribute our proprietary CRISPR/Cas9 gene editing technology and intellectual property. Bayer Healthcare will also provide up to $300.0 million in research and development investments to the JV over the first five years.

In connection with the JV Agreement, we will receive a technology access fee of $35.0 million. In January 2016, we also issued a convertible loan to Bayer Global Investments B.V., or Bayer BV, for gross proceeds of $35.0 million which was immediately converted to Series B Preferred Shares at a conversion price of $44.78 per share. On February 12, 2016, we and Bayer Healthcare completed the formation of the Joint Venture entity, Casebia Therapeutics LLP. In connection with the JV Agreement, Bayer BV also agreed to purchase $35.0 million of our common shares in a private placement upon the successful completion of an initial public offering of our common shares at the price paid by other investors in the initial public offering. The JV is led by Dr. Axel Bouchon, Head of the Bayer Life Science Center, on an interim basis as general manager, while Dr. Rodger Novak, our Chief Executive Officer, is the interim chairman of the management board of the JV.

Financial Overview

Revenue

To date, we have not generated any revenue from product sales and do not expect to do so in the near future. During the year ended December 31, 2015, we recognized $0.2 million of revenue related to our collaboration agreement with Vertex. As of December 31, 2015, we had not received any milestone or royalty payments under the Vertex collaboration agreement. For additional information about our revenue recognition policy, see the “Critical Accounting Policies and Estimates—Revenue.”

For the foreseeable future, we expect substantially all of our revenue to be generated from our collaboration with Vertex, our joint venture with Bayer Healthcare and any other collaboration agreements we may enter into.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our product discovery efforts and the development of our product candidates, which include:

- employee-related expenses, including salaries, benefits and equity-based compensation expense;
- costs of services performed by third parties that conduct research and development and preclinical activities on our behalf;
- costs of purchasing lab supplies and non-capital equipment used in our preclinical activities and in manufacturing preclinical study materials;
- consultant fees;
- facility costs, including rent, depreciation and maintenance expenses; and
- fees for acquiring and maintaining licenses under our third-party licensing agreements.

Research and development costs are expensed as incurred. Nonrefundable advance payments for research and development goods or services to be received in the future are deferred and capitalized. The capitalized

amounts are expensed as the related goods are delivered or the services are performed. At this time, we cannot reasonably estimate or know the nature, timing or estimated costs of the efforts that will be necessary to complete the development of any product candidates we may identify and develop. This is due to the numerous risks and uncertainties associated with developing such product candidates, including the uncertainty of:

- successful completion of preclinical studies and Investigational New Drug-enabling studies;
- successful enrollment in, and completion of, clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity;
- launching commercial sales of the product, if and when approved, whether alone or in collaboration with others;
- acceptance of the product, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies and treatment options;
- a continued acceptable safety profile following approval;
- enforcing and defending intellectual property and proprietary rights and claims; and
- achieving desirable medicinal properties for the intended indications.

A change in the outcome of any of these variables with respect to the development of any product candidates we may develop could significantly change the costs, timing and viability associated with the development of that product candidate.

Except for activities we perform in connection with our collaboration with Vertex, we do not track research and development costs on a program-by-program basis. We plan to track research and development costs for individual development programs when we identify a product candidate from the program that we believe we can advance into clinical trials. We incurred $0.3 million of research and development expense during the year ended December 31, 2015 related to the collaboration with Vertex.

Research and development activities are central to our business model. We expect research and development costs to increase significantly for the foreseeable future as our current development programs progress and new programs are added.

General and Administrative Expenses

General and administrative expenses consist primarily of employee related expenses, including salaries, benefits, and equity-based compensation, for personnel in executive, finance, accounting, business development and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters, and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future to support continued research and development activities, potential commercialization of our product candidates and increased costs of operating as a public company. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses. We also anticipate increased expenses related to the reimbursements of third-party patent related expenses in connection with the ongoing interference proceeding with respect to our in-licensed intellectual property. Additionally, we

anticipate increased costs associated with being a public company, including expenses related to services associated with maintaining compliance with exchange listing and Securities and Exchange Commission, or the SEC, requirements, insurance costs and investor relations costs.

Results of Operations

Comparison of the Years Ended December 31, 2014 and 2015

The following table summarizes our results of operations for the years ended December 31, 2014 and 2015, together with the dollar change in those items:

	Year Ended December 31,		Period-to-Period Change
	2014	2015	
	(in thousands of dollars)		
Collaboration revenue	$ —	$ 247	$ 247
Operating expenses:			
Research and development	1,513	12,573	11,060
General and administrative	5,114	13,403	8,289
Total operating expenses	6,627	25,976	19,349
Loss from operations	(6,627)	(25,729)	(19,102)
Other expense, net	(236)	(92)	144
Net loss before benefit from income taxes	(6,863)	(25,821)	(18,958)
Benefit from (provision for) income taxes	63	(7)	(70)
Net loss	$(6,800)	$(25,828)	$ (19,028)

Collaboration Revenue

We recognized collaboration revenue during the year ended December 31, 2015 of $0.2 million, related to our collaboration agreement with Vertex. We did not record any revenue during the year ended December 31, 2014.

Research and Development Expenses

Research and development expenses increased by $11.1 million to $12.6 million for the year ended December 31, 2015, from $1.5 million for the year ended December 31, 2014. The increase in research and development expenses was primarily attributable to an increase in employee costs of $4.8 million associated with salaries, benefits and equity-based compensation expenses from hiring additional personnel, an increase in professional service expense of $2.0 million, an increase in facilities expense of $2.3 million, principally associated with the establishment in February 2015 of our research and development center in Cambridge, Massachusetts, and an increase in licensing fees of $1.4 million.

General and Administrative Expenses

General and administrative expenses increased by $8.3 million to $13.4 million for the year ended December 31, 2015, from $5.1 million for the year ended December 31, 2014. The increase in general and administrative expenses was primarily attributable to increase in employee costs of $1.9 million associated with salaries, benefits and equity-based compensation expenses from hiring additional senior personnel, increased consulting and professional fees of $3.2 million, including directors' fees, audit and accounting fees, and consultant fees; and increased intellectual property costs of $1.9 million, including third-party costs to procure the issuance of patents in jurisdictions outside the United States and costs related to the ongoing interference proceedings with respect to our in-licensed intellectual property.

Other Expense, Net

Other expense, net decreased by $0.1 million for the year ended December 31, 2015 due to a decrease in the loss on foreign currency remeasurement of $0.2 million, offset by an increase in non-cash interest expense related to the convertible notes of $0.1 million.

Liquidity and Capital Resources

Overview

From our inception through December 31, 2015, we raised an aggregate of $177.5 million, of which $64.3 million consisted of gross proceeds from private placements of preferred shares, $38.2 million from the issuance of convertible notes and an up-front payment under our collaboration agreement with Vertex of $75.0 million. As of December 31, 2015, we had $156.0 million in cash of which approximately $155.5 million was held outside of the United States.

Preferred Share Financing

In October 2013, we issued 132,000 Series A-1 Preferred Shares for CHF 3.80 ($4.25) per share, resulting in gross proceeds of CHF 0.5 million ($0.6 million). Pursuant to the terms of the Shareholders' Agreement between us and the holders of the Series A-1 Preferred Shares, the holders of the Series A-1 Preferred Shares had the right to purchase an additional 394,737 Series A-1 Preferred Shares at CHF 3.80 ($4.25) per share, or the Series A-1 Tranche Rights. In connection with the issuance of the Series A-2 Preferred Shares, the Series A-1 Tranche Rights were terminated without exercise in April 2014.

In April 2014, the Company issued 936,000 Series A-2 Preferred Shares in exchange for CHF 10.162 ($11.57) per share whereby CHF 4.82 ($5.49) per share was received upon issuance resulting in gross proceeds of CHF 4.5 million ($5.1 million) and the balance of CHF 5.342 ($6.08) per share was callable by our board of directors upon the occurrence of certain conditions. In February 2015, our board of directors called the remaining amounts to be invested under the Series A-2 Agreement resulting in additional gross proceeds of CHF 5.0 million ($5.3 million).

In April 2015, we issued 3,227,401 Series A-3 Preferred Shares in exchange for $14.16 per share whereby $7.08 per share was received upon issuance, resulting in gross proceeds of $22.8 million, and the balance of $7.08 per share was due upon the occurrence of certain milestones. As of December 31, 2015, none of the milestones had occurred and we had an outstanding subscription receivable of $22.8 million related to the Series A-3 Preferred Shares. In May 2016, our board of directors determined that the milestones had been achieved and called the remaining $22.8 million. When received, this will result in additional gross proceeds of $22.8 million.

In May 2015, we issued 1,355,704 Series B Preferred Shares in exchange for CHF 20.6535 ($22.47) per share resulting in gross proceeds of CHF 28.0 million ($30.5 million).

Convertible Loan Financing

On October 26, 2015, we entered into a Convertible Loan Agreement with Vertex and certain existing shareholders, or the Convertible Loan, under which we could borrow up to $40.0 million. The Convertible Loan accrued interest at 2.5% per annum and had an initial maturity date of April 26, 2016, subject to acceleration upon the occurrence of certain conditions stated in the Convertible Loan. On various dates between November 23, 2015 and December 7, 2015, we issued the Convertible Loan in exchange for aggregate net proceeds of $38.2 million. On January 29, 2016, all of the outstanding principal plus accrued interest under the Convertible Loan was automatically converted into 857,783 Series B Preferred Shares at a conversion price of $44.78 per share.

Funding Requirements

Our primary uses of capital are, and we expect will continue to be, research and development services, compensation and related expenses, laboratory and related supplies, legal and other regulatory expenses, patent prosecution filing and maintenance costs for our licensed intellectual property and general overhead costs. We expect our expenses to increase compared to prior periods in connection with our ongoing activities, particularly as we continue research and development and preclinical activities and as we begin to occupy our new office and laboratory facility. In addition, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company.

Because our research programs are still in preclinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of any future product candidates or whether, or when, we may achieve profitability. Until such time, as we can generate substantial product revenues, if ever, we expect to finance our cash needs through a combination of equity or debt financings and collaboration arrangements. We are entitled to technology access fees and research payments under our collaboration with Vertex and the JV. Additionally, we are eligible to earn payments, in each case, on a per-product basis under the JV Agreement with Bayer Healthcare and our collaboration with Vertex. Except for these sources of funding, upon completion of this offering, we will not have any committed external source of liquidity. To the extent that we raise additional capital through the future sale of equity or debt securities, the ownership interest of our shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing shareholders. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Outlook

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that the net proceeds from this offering and the upfront payment and concurrent private placement with Bayer BV, together with our existing cash, will enable us to fund our operating expenses and capital expenditures for at least the next 24 months, without giving effect to any additional proceeds we may receive under our collaboration agreements with Vertex and Bayer AG and its subsidiaries, or Bayer. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect.

Our ability to generate revenue and achieve profitability depends significantly on our success in many areas, including: developing our delivery technologies and our CRISPR/Cas9 technology platform; selecting appropriate product candidates to develop; completing research and preclinical and clinical development of selected product candidates; obtaining regulatory approvals and marketing authorizations for product candidates for which we complete clinical trials; developing a sustainable and scalable manufacturing process for product candidates; launching and commercializing product candidates for which we obtain regulatory approvals and marketing authorizations, either directly or with a collaborator or distributor; obtaining market acceptance of our product candidates; addressing any competing technological and market developments; negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter; maintaining good relationships with our collaborators and licensors; maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and attracting, hiring and retaining qualified personnel.

Cash Flows

Comparison of the Years Ended December 31, 2014 and 2015

The following table provides information regarding our cash flows for the years ended December 31, 2014 and 2015:

	Year Ended December 31,	
	2014	2015
	(in thousands of dollars)	
Net cash (used in) provided by operating activities	$ (4,793)	$ 59,428
Net cash used in investing activities	—	(1,154)
Net cash provided by financing activities	5,123	96,733
Effect of exchange rate changes on cash	254	9
Net increase in cash and cash equivalents	$ 584	$ 155,016

Net Cash (Used in) Provided by Operating Activities

Net cash provided by operating activities was $59.4 million for the year ended December 31, 2015 and consisted primarily of an increase in deferred revenue of $75.1 million from upfront payments received in connection with the collaboration agreement with Vertex along with an increase in accounts payable and accrued expenses of $7.7 million, partially offset by net loss of $25.8 million adjusted for non-cash items (including equity-based compensation expense of $3.7 million, non-cash interest expense of $0.1 million, and depreciation and amortization expense of $0.1 million), an increase in prepaid expenses and other current assets of $1.0 million, and an increase in restricted cash to secure letters of credit related to our facility lease in Cambridge, Massachusetts, of $0.7 million.

Net cash used in operating activities was $4.8 million for the year ended December 31, 2014 and consisted primarily of a net loss of $6.8 million adjusted for non-cash items (including equity-based compensation expense of $0.7 million, amortization expense of $38,000 and foreign currency remeasurement loss of $0.3 million), along with an increase in accounts payable and accrued expenses of $1.6 million.

Net Cash Used in Investing Activities

Net cash used in investing activities was $1.2 million during the year ended December 31, 2015, compared to $0 during the year ended December 31, 2014, an increase of $1.2 million, which resulted from the purchase of property and equipment of $1.2 million primarily associated with the commencement of internal research and development operations in Cambridge, Massachusetts. We expect purchases of property and equipment to continue to increase in each of 2016 and 2017 as we build-out and outfit the office and laboratory space we expect to occupy beginning in 2017.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was $96.7 million for the year ended December 31, 2015, compared to $5.1 million for the year ended December 31, 2014. The cash provided by financing activities for the year ended December 31, 2015 primarily consisted of net proceeds of $5.3 million related to a subscription receivable for Series A-2 Preferred Shares, $22.9 million from the issuance of Series A-3 Preferred Shares, $30.5 million from the issuance of Series B Preferred Shares, and $38.2 million from the issuance of a convertible loan. The cash provided by financing activities for the year ended December 31, 2014 primarily consisted of net proceeds of $5.1 million from the issuance of Series A-2 Preferred Shares.

Contractual Obligations

The following table summarizes our significant contractual obligations as of December 31, 2015:

	Payments due by period				
	Total	Less than 1 Year	1 - 3 Years	3 - 5 Years	More than 5 Years
	(in thousands of dollars)				
Operating lease obligations(1)	$ 8,600	$ 1,291	$ 2,722	$ 2,887	$ 1,700
Licensing agreement(2)	130	26	52	52	—
Sponsored research agreements	1,795	1,230	565	—	—
Total contractual cash obligations	$10,525	$ 2,547	$ 3,339	$ 2,939	$ 1,700

(1) Represents future minimum lease payments under our non-cancelable operating leases. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

(2) Represents perpetual licensing and patent assignment agreement with one of our founders. As the agreement end date is undetermined, we have not included an amount for the "More than 5 Years" criteria.

The table above does not include $56.5 million related to two leases for office and laboratory space entered into subsequent to December 31, 2015. Additionally, the table above does not include potential milestone fees, sublicense fees, royalty fees, licensing maintenance fees, and reimbursement of patent maintenance costs that we may be required to pay under agreements we have entered into to license intellectual property. We have not included such potential milestone royalty obligations in the table above because they are contingent upon the occurrence of future events and the timing and likelihood of such potential obligations are not known with certainty. We have not included our obligation to pay patent prosecution filing and maintenance costs for intellectual property licensed from Dr. Emmanuelle Charpentier as such costs cannot be reliably estimated until incurred. For further information regarding these agreements and amounts that could become payable in the future under these agreements, please see the section of this prospectus titled "Business—License Agreements."

We enter into agreements in the normal course of business with vendors for preclinical research studies and other services and products for operating purposes. We have not included these payments in the table of contractual obligations above since the contracts are cancelable at any time by us, generally upon 30 days prior written notice to the vendor, and therefore we believe that our non-cancelable obligations under these agreements are not material.

In May 2016, we entered into an agreement to sublease office and laboratory space in Cambridge, Massachusetts, for an initial term of ten years with an option to extend the lease for an additional five years. Our contractual obligation related to lease payments over the term of the sublease is approximately $56.2 million commencing in February 2017.

We have engaged several research institutions to identify new delivery strategies and applications of the CRISPR/Cas9 technology. As a result of these efforts, we have agreed to sponsor three research programs during 2016, with one of these continuing through 2018.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Critical Accounting Policies and Significant Judgments and Estimates

This discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. We

believe that several accounting policies are important to understanding our historical and future performance. We refer to these policies as critical because these specific areas generally require us to make judgments and estimates about matters that are uncertain at the time we make the estimate, and different estimates—which also would have been reasonable—could have been used. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and other market-specific or other relevant assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements included elsewhere in this prospectus, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Revenue

We recognize revenue for each unit of accounting when all of the following criteria are met: (i) persuasive evidence of an arrangement exists, (ii) delivery has occurred or services have been rendered, (iii) the seller's price to the buyer is fixed or determinable and (iv) collectability is reasonably assured.

The terms of our collaboration and license agreements contain multiple deliverables, which include licenses to CRISPR/Cas9-based therapeutic products directed to specific targets, referred to as exclusive licenses, as well as research and development activities to be performed by us on behalf of the collaboration partner related to the licensed targets. Payments that we may receive under these agreements include nonrefundable technology access fees, payments for research activities, payments based upon the achievement of specified milestones and royalties on any resulting net product sales.

Multiple Element Arrangements

We evaluate multiple-element arrangements to determine (i) the deliverables included in the arrangement and (ii) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. When deliverables are separable, consideration received is allocated to the separate units of accounting based on the relative selling price method and the appropriate revenue recognition principles are applied to each unit. When we determine that an arrangement should be accounted for as a single unit of accounting, we must determine the period over which the performance obligations will be performed and revenue will be recognized. This evaluation requires us to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that (i) the delivered item has value to the customer on a standalone basis and (ii) the arrangement includes a general right of return with respect to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in our control. In assessing whether an item has standalone value, we consider factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, we consider whether the collaboration partner can use any other deliverable for its intended purpose without the receipt of the remaining deliverable, whether the value of the deliverable is dependent on the undelivered item, and whether there are other vendors that can provide the undelivered items.

The consideration received under an arrangement that is fixed or determinable is then allocated among the separate units of accounting based on the relative selling prices of the separate units of accounting. We determine the selling price of a unit of accounting within each arrangement using (i) vendor-specific objective evidence of selling price, if available; (ii) third-party evidence of selling price if vendor-specific objective evidence is not available; or (iii) best estimate of selling price, if neither vendor-specific objective evidence nor third-party evidence is available. Determining the best estimate of selling price for a unit of accounting requires significant

judgment. In developing the best estimate of selling price for a unit of accounting, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. We validate the best estimate of selling price for units of accounting by evaluating whether changes in the key assumptions used to determine the best estimate of selling price will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

We recognize arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria are satisfied for that particular unit of accounting. In the event that a deliverable does not represent a separate unit of accounting, we recognize revenue from the combined unit of accounting over the contractual or estimated performance period for the undelivered items, which is typically the term of our research and development obligations. If there is no discernible pattern of performance or objectively measurable performance measures do not exist, then we recognize revenue under the arrangement on a straight-line basis over the period we are expected to complete our performance obligations. Conversely, if the pattern of performance over which the service is provided to the customer can be determined and objectively measurable performance measures exist, then we recognize revenue under the arrangement using the proportional performance method. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method or proportional performance method, as applicable, as of the period ending date.

Significant management judgment is required in determining the level of effort required under an arrangement and the period over which we are expected to complete our performance obligations under an arrangement. Steering committee services that are not inconsequential or perfunctory and that are determined to be performance obligations are combined with other research services or performance obligations required under an arrangement, if any, in determining the level of effort required in an arrangement and the period over which we expect to complete our aggregate performance obligations.

Recognition of Milestones and Royalties

Our collaboration and license agreements include contingent milestone payments related to specific development, regulatory and sales-based milestones. Development and regulatory milestones are typically payable when a product candidate initiates or advances in clinical trial phases, upon submission for marketing approval with regulatory authorities, and upon receipt of actual marketing approvals for a therapeutic or for additional indications. Sales-based milestones are typically payable when annual sales reach specified levels.

We evaluate whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (i) the consideration is commensurate with either our performance to achieve the milestone or the enhancement of the value of the delivered item as a result of a specific outcome resulting from our performance to achieve the milestone, (ii) the consideration relates solely to past performance and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone and the level of effort and investment required to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. We will recognize revenue in its entirety upon successful accomplishment of any substantive milestones, assuming all other revenue recognition criteria are met. Milestones that are not considered substantive are recognized as earned if there are no remaining performance obligations or over the remaining period of performance, with a cumulative catch-up being recognized for the elapsed portion of the period of performance, assuming all other revenue recognition criteria are met.

Nonrefundable research, development and regulatory milestones that are expected to be achieved as a result of our efforts during the period of our performance obligations under the collaboration and license agreements are generally considered to be substantive and are recognized as revenue upon the achievement of the milestone,

assuming all other revenue recognition criteria are met. If not considered to be substantive, revenue from achievement of milestones is initially deferred and recognized over the remaining term of our performance obligations. Milestones that are not considered substantive because we do not contribute effort to their achievement are recognized as revenue upon achievement, assuming all other revenue recognition criteria are met, as there are no undelivered elements remaining and no continuing performance obligations on our part.

Amounts received prior to satisfying the revenue recognition criteria listed above are recorded as deferred revenue in the accompanying balance sheets. Although we follow detailed guidelines in measuring revenue, certain judgments affect the application of our revenue policy. For example, in connection with our existing collaboration agreement, we have recorded on the balance sheet short-term and long-term deferred revenue based on our best estimate of when such revenue will be recognized. However, this estimate is based on our current research plan and, if our research plan should change in the future, we may recognize a different amount of deferred revenue over the following 12-month period.

The estimate of deferred revenue also reflects management's estimate of the periods of our involvement in the collaboration. Our primary performance obligations under this collaboration consist of research and development services. In certain instances, the timing of satisfying these obligations can be difficult to estimate. Accordingly, our estimates may change in the future. Such changes to estimates would result in a change in prospective revenue recognition amounts. If these estimates and judgments change over the course of our collaborative agreement, it may affect the timing and amount of revenue that we will recognize and record in future periods.

Variable Interest Entities

We review each legal entity formed by parties related to the Company to determine whether or not the entity is a Variable Interest Entity, or VIE, in accordance with FASB ASC Topic 810, Consolidation. If the entity is a VIE, we assesses whether or not we are the primary beneficiary of that VIE based on a number of factors, including (i) which party has the power to direct the activities that most significantly affect the VIE's economic performance, (ii) the parties' contractual rights and responsibilities pursuant to any contractual agreements and (iii) which party has the obligation to absorb losses or the right to receive benefits from the VIE. If we determine that we are the primary beneficiary of a VIE, we treat the VIE as a business combination and consolidate the financial statements of the VIE into our consolidated financial statements at the time that determination is made. On a quarterly basis, we evaluate whether it continues to be the primary beneficiary of any consolidated VIEs. If we determine that we are no longer the primary beneficiary of a consolidated VIE, or no longer have a variable interest in the VIE, we deconsolidate the VIE in the period that the determination is made.

If we determine that we are the primary beneficiary of a VIE that meets the definition of a business, we measure the assets, liabilities and non-controlling interests of the newly consolidated entity at fair value in accordance with FASB ASC Topic 805, Business Combinations on the date we become the primary beneficiary.

For the years ended December 31, 2014 and 2015, we consolidated the financial statements of TRACR into our consolidated financial statements as a VIE. See Note 4 to the consolidated financial statements for further details relating to the consolidation of TRACR as a VIE.

Equity-Based Compensation

We measure equity-based awards to employees and members of the board of directors based on the grant-date fair value of those awards and recognize equity-based compensation expense, net of estimated forfeitures, on a straight-line basis over the requisite service period which is generally the vesting period of the award. In developing a forfeiture rate estimate, we considered our historical experience with pre-vesting forfeitures for service-based awards. We estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from those estimates.

We measure equity-based awards to consultants and non-employees based on the fair value on the grant date. Compensation expense is recognized over the period during which services are rendered by such consultants and non-employees until completed. At the end of each financial reporting period prior to completion of such services, the fair value of these awards is remeasured using the then-current fair value of the award.

We classify equity-based compensation expense in our consolidated statement of operations in the same manner in which the award recipient's salary and related costs are classified or in which the award recipient's service payments are classified.

Our restricted share awards are subject to contingent repurchase features which allows the Company to repurchase unvested shares if certain contingent events outside of the control of the Company occur. At no time during 2014 or 2015 were these events deemed probable of occurring, and as such, the awards are not subject to liability accounting.

Determination of Fair Value of Common Shares on Grant Dates

As there has been no public market for our equity instruments to date, the estimated fair value of our common shares has been determined by our board of directors as of the grant date, with input from management, considering our most recently available third-party valuations of common shares and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Our common share valuations were prepared using either an option-pricing method, or OPM, or a probability-weighted expected return method, or PWERM, which used a combination of market approaches and an income approach to estimate our enterprise value. The OPM treats common securities and preferred securities as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common shares have value only if the funds available for distribution to members are expected to exceed the value of the preferred security liquidation preference at the time of the liquidity event, such as a strategic sale or a merger. The PWERM is a scenario-based methodology that estimates the fair value of common shares based upon an analysis of future values for the company, assuming various outcomes. The common share values are based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of common and preferred securities. The future value of the common shares under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common shares. These third-party valuations were performed at various dates, which resulted in the following valuations of our common shares:

Valuation Date	Fair Value of Common Shares
November 5, 2013	$ 1.35
April 14, 2014	$ 5.06
April 15, 2015	$ 6.89
September 10, 2015	$ 13.04
November 4, 2015	$ 18.66
December 17, 2015	$ 19.14

In addition to considering the results of these third-party valuations, our board of directors considered various objective and subjective factors to determine the fair value of our common shares as of each grant date, including:

- the prices of our preferred shares sold to or exchanged between outside investors in arm's length transactions, and the rights, preferences and privileges of our preferred shares as compared to those of our common shares, including the liquidation preferences of our preferred shares;
- the progress of our research and development efforts, including the status of preclinical studies for our product candidates;
- the lack of liquidity of our equity as a private company;
- our stage of development and business strategy and the material risks related to our business and industry;
- the achievement of enterprise milestones, including entering into collaboration agreements;
- the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;
- any external market conditions affecting the biotechnology industry, and trends within the biotechnology industry;
- the likelihood of achieving a liquidity event for the holders of our common shares, such as an initial public offering, or IPO, or a sale of our company, given prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our equity-based compensation expense could be materially different.

Following the closing of this offering, the fair value of our common shares will be determined based on the quoted market price.

Equity-based Award Grants

The following table summarizes by grant date the number of restricted common shares and common shares issuable upon exercise of options granted between January 1, 2015 and December 31, 2015, the per share purchase or exercise prices, the fair value of the common shares on the grant dates, and the estimated fair value per share utilized to calculate equity-based compensation expense.

Grant Date	Share Pool	Type of Award	Number of Shares	Purchase or Exercise Price per Share	Fair Value of Common Shares on Grant Date (1)	Retrospective Fair Values of Common Shares on Grant Date (2)	Estimated Fair Values Per Share of Awards on Grant Date
April 1, 2015	Crispr AG	Common Shares	255,854	$ —	$ 6.24	$ 6.98	$ 6.98
April 1, 2015	Crispr AG	Restricted Share Awards	196,809	$ —	$ 6.24	$ 6.98	$ 6.98
May 7, 2015	2015 Option Plan	Options	18,843	$ 6.55	$ 6.55	$ 7.33	$ 5.13
September 10, 2015	Fay Corp.	Restricted Share Awards	227,761	$ —	$ 6.15	$ 13.04	$ 13.04
September 10, 2015	2015 Option Plan	Restricted Share Awards	40,214	$ 6.15	$ 6.15	$ 13.04	$ 6.89
September 10, 2015	2015 Option Plan	Options	492,180	$ 6.15	$ 6.15	$ 13.04	$ 10.20-11.62
November 4, 2015	2015 Option Plan	Options	58,476	$ 18.66	$ 18.66	$ 18.66	$ 12.71
December 17, 2015	2015 Option Plan	Options	12,500	$ 19.14	$ 19.14	$ 19.14	$ 13.04
December 17, 2015	2015 Option Plan	Restricted Share Awards	2,624	$ —	$ 19.14	$ 19.14	$ 19.14

(1) Represents the determination by our board of directors of the fair value of our common stock on the date of grant, taking into consideration the various objective and subjective factors described below.

(2) The fair value of common shares at the grant date was adjusted in connection with a retrospective fair value assessment for financial reporting purposes.

Equity-based compensation expense totaled approximately $0.7 million and $3.7 million for the years ended December 31, 2014 and 2015. As of December 31, 2015, we had $4.3 million of unrecognized compensation expense related to stock option awards, which are expected to be recognized over weighted-average remaining vesting periods of approximately 3.3 years. As of December 31, 2015, we had $4.7 million of unrecognized compensation expense related to restricted share awards, which are expected to be recognized over weighted-average remaining vesting periods of approximately 2.6 years. We expect the impact of our equity-based compensation expense for restricted shares and options to purchase common shares granted to employees and non-employees to grow in future periods due to the potential increases in the value of our common shares and headcount.

JOBS Act

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an "emerging growth company," or an EGC, can take advantage of the extended transition period for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an EGC, we intend to rely on certain of these exemptions, including exemptions from the requirement to provide an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act, SOX, and from any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an EGC until the earlier of: (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more, (ii) the last day of the fiscal year following the fifth anniversary of the date of the completion of this offering, (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

Recent Accounting Pronouncements

Refer to Note 2, "Summary of Significant Accounting Policies," in the accompanying notes to the consolidated financial statements for a discussion of recent accounting pronouncements. There were no new accounting pronouncements adopted during 2015 that had a material effect on our financial statements.

Qualitative and Quantitative Disclosures about Market Risk

Foreign Exchange Market Risk

As a result of our foreign operations, we face exposure to movements in foreign currency exchange rates, primarily the Swiss Franc and British Pound, against the U.S. dollar. The current exposures arise primarily from cash, accounts payable, and intercompany receivables and payables.

Taxation

We are subject to corporate taxation in Switzerland.

We are also entitled under Swiss laws to carry forward any losses incurred for a period of seven years and can offset our losses carried forward against future profits. As of December 31, 2015, we reported tax loss carry forwards from inception through 2015 for purposes of Swiss federal direct taxes in the aggregate amount of

CHF 22.0 million. Due to the expected mixed company status (in case the advance tax ruling with respect to the mixed company status will be accepted) the tax losses at cantonal level amount to CHF 4.1 million. These tax losses could be available to offset future taxable income. If not used, these tax losses will expire seven years after the year in which they were incurred. Due to our limited income, there is a high risk that the tax loss carry forwards will expire partly or entirely.

The corporate profit tax rate in the Canton of Basel-Stadt where we are domiciled amounts currently to a maximum of 20%. We applied for a tax privilege as mixed company for the years 2014 and 2015, and this application is pending. The Cantonal corporate profit tax rate for mixed companies is between 8% and 14%. The Canton does from time to time amend the level of taxation levied on corporations and there is no certainty that the tax rate currently in effect will not change in the future. If and when the corporate tax reform III will enter into force, the mixed company privilege will be abolished within a period of two years and corporate tax rates will be adapted.

BUSINESS

You should read the following discussion together with our consolidated financial statements and related notes and other financial information appearing in this prospectus. Some of the information contained in this discussion or set forth elsewhere in this prospectus includes forward-looking statements that involve risks and uncertainties. You should review the sections of this prospectus captioned "Risk Factors" and "Special Note Regarding Forward-Looking Statements" for a discussion of important factors that could cause our actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a leading gene editing company focused on the development of CRISPR/Cas9-based therapeutics. CRISPR/Cas9 stands for Clustered, Regularly Interspaced Short Palindromic Repeats (CRISPR) Associated protein-9 and is a revolutionary gene editing technology that allows for precise, directed changes to genomic DNA. We are applying this technology to treat a broad set of rare and common diseases by disrupting, correcting or regulating disease-related genes. We believe that our scientific expertise, together with our approach, may enable an entirely new class of highly effective and potentially curative treatments for patients for whom current biopharmaceutical approaches have had limited success. Our most advanced programs target beta-thalassemia and sickle cell disease, two hemoglobinopathies that have high unmet medical need.

The use of CRISPR/Cas9 for gene editing was derived from a naturally occurring viral defense mechanism in bacteria and has been described by leading scientific journals as a breakthrough technology. The application of CRISPR/Cas9 for gene editing was co-invented by one of our scientific founders, Dr. Emmanuelle Charpentier, a director of the Max Planck Institute for Infection Biology in Berlin. Dr. Charpentier and her collaborators published work elucidating the mechanism by which the Cas9 endonuclease, a key component of CRISPR/Cas9, can be programmed to cut double-stranded DNA at specific locations. We have acquired rights to the foundational intellectual property encompassing CRISPR/Cas9 and related technologies from Dr. Charpentier, and continue to strengthen our intellectual property estate through our own research and additional in-licensing efforts, furthering our leadership in the development of CRISPR/Cas9-based therapeutics.

Our product development and partnership strategies are designed to exploit the full potential of the CRISPR/Cas9 platform while maximizing the probability of successfully developing our product candidates. We are pursuing a two-pronged product development strategy utilizing both *ex vivo* and *in vivo* approaches. Our most advanced programs use an *ex vivo* approach, whereby cells are harvested from a patient, treated with a CRISPR/Cas9-based therapeutic and reintroduced. We believe that an *ex vivo* approach is less technically challenging than an *in vivo* approach. We have chosen to conduct our lead programs in hemoglobinopathies given the relative ease of editing genes *ex vivo*, the significant unmet medical need associated with beta-thalassemia and sickle cell disease and the well-understood genetics of these diseases. Beyond these lead programs, we are pursuing a number of additional *ex vivo* applications, as well as select *in vivo* applications, whereby the CRISPR/Cas9 therapeutic is delivered directly to target cells within the human body. Our initial *in vivo* applications will leverage well-established delivery technologies for gene-based therapeutics.

Given the numerous potential therapeutic applications for CRISPR/Cas9, we have partnered strategically to broaden the indications we can pursue and accelerate development of programs by accessing specific disease-area expertise. In particular, we established a collaboration with Vertex Pharmaceuticals, Incorporated, or Vertex, and a joint venture with Bayer AG and its subsidiaries, or Bayer, in order to pursue specific indications where these companies have outstanding and distinctive capabilities. The significant resource commitments by our partners underscore the potential of our platform, as well as their dedication to developing transformative CRISPR/Cas9-based treatments.

Our mission is to create transformative gene-based medicines for serious human diseases. We believe that our highly experienced team, together with our scientific expertise, differentiated product development strategy, partnerships and intellectual property position us as a leader in the development of CRISPR/Cas9-based therapeutics.

Our Team

We have assembled a management team with years of highly relevant experience to enable the development of our gene editing platform and the advancement of our product candidates. This team has extensive expertise in drug discovery and development, clinical and regulatory strategy, as well as business strategy and operations. Some of our key team members include:

- ***Rodger Novak, M.D., our Co-Founder and Chief Executive Officer,*** who brings over a decade of extensive preclinical and clinical development experience from his previous biopharma roles. His prior positions include Global Head of Anti-Infectives Research and Development at Sanofi, co-founder and Chief Operating Officer of Nabriva Therapeutics AG, Deputy Head of the Sandoz GmbH Antibiotic Research Institute, and his role as a Professor of Microbiology at the Vienna Biocenter in Austria.
- ***Sven Ante (Bill) Lundberg, M.D., our Chief Scientific Officer,*** who brings wide-ranging expertise across all phases of drug development from his more than 15 years of experience in the life sciences industry. These include his most recent position as the Vice President and Head of Translational Medicine at Alexion Pharmaceuticals Inc., where he was responsible for all research and development efforts, from discovery to clinical proof-of-concept, and previous leadership positions at Taligen Therapeutics, Inc., Wyeth and Genzyme Corporation.
- ***Samarth Kulkarni, Ph.D., our Chief Business Officer,*** previously a Partner at McKinsey & Company where he co-led the biotechnology practice and advised leading biopharmaceuticals companies on strategic and business development matters.

Our management team is actively advised by a six-member scientific advisory board, which includes our co-founder, Dr. Emmanuelle Charpentier. We have assembled a team of advisors with know-how in complementary disciplines necessary for the development of our CRISPR/Cas9 product candidates. Our advisors are considered renowned leaders in delivery technologies, mechanisms of DNA repair, stem cell engineering, gene silencing and CRISPR/Cas9 gene editing. We believe that our advisory board's expertise is a pivotal asset for our product development efforts.

Our Strategy

Our objective is to be a leader in the development of novel CRISPR/Cas9-based therapeutics, and to create transformative treatments for unaddressed or under-addressed human diseases. Key components of our strategy include:

- **Focus on the Hematopoietic System Through *Ex Vivo* Approaches.**
  - ***Rapidly Advance Lead Programs in Hemoglobinopathies*.** Our hemoglobinopathy programs employ an *ex vivo* gene editing strategy, supported by well-understood genetics and target patient populations with a high unmet medical need, making these programs suitable for rapid advancement through clinical development. We aim to initiate our first clinical trial for these programs in late 2017.
  - ***Apply Our Hematopoietic Gene Editing Capabilities in Other Indications.*** There are numerous diseases that are potentially treatable through *ex vivo* gene editing of the hematopoietic system. We plan to apply the capabilities we are developing in hemoglobinopathies to treat other diseases. We have launched programs in two such diseases, severe combined immunodeficiency disease, or SCID, and Hurler syndrome, a

genetic metabolic disorder. In addition, we are utilizing our *ex vivo* gene editing expertise to advance our efforts in cell therapies for immuno-oncology applications.

- **Pursue Select Indications Requiring *In Vivo* Approaches**.
  - ***Target the Liver Using Readily Available Delivery Technologies.*** Clinically-validated viral and non-viral approaches for delivery of gene-based therapeutics to the liver are available today and we believe they are suitable for use in CRISPR/Cas9 therapeutics. We intend to customize and use these delivery technologies for programs in hemophilia and genetic diseases of liver metabolism, including Glycogen Storage Disease Ia, or GSDIa. We are developing these programs in parallel with our *ex vivo* therapeutic candidates.
  - ***Optimize Delivery Technologies to Target Select* In Vivo *Indications Outside the Liver.*** We intend to pursue select *in vivo* programs targeting diseases such as Duchenne muscular dystrophy and cystic fibrosis, both of which have significant patient populations with high unmet medical need and, we believe, are well suited for our CRISPR/Cas9 gene editing platform. We are working internally, as well as through third-party collaborations, to optimize viral and non-viral delivery technologies for use in these diseases.
- **Continue to Foster and Strategically Leverage Our Collaborations with Bayer and Vertex.**
  - Our collaborations will allow us to pursue additional indications by utilizing the extensive disease-area expertise and resources of our collaborators. Our joint venture with Bayer HealthCare LLC, or Bayer Healthcare, leverages their expertise in disease areas such as hemophilia and ophthalmology, as well as validated disease models access to key opinion leaders. We are targeting cystic fibrosis with Vertex, which brings leading drug development capabilities and clinical relationships for this disease.
- **Advance our Leading Position in the Field of Gene Editing.**
  - We are continually investing in the enhancement of our CRISPR/Cas9 platform. Through our investments, we seek to optimize the various components, such as the Cas9 protein, gene correction and repair mechanisms and CRISPR/Cas9 delivery vehicles. We will invest both internally and through our existing and potential future collaborations to advance our technology.

Gene Editing Background

There are thousands of diseases caused by aberrant DNA sequences. Traditional small molecule and biologic therapies have had limited success in treating many of these diseases because they fail to address the underlying genetic causes. Newer approaches such as RNA therapeutics and viral gene therapy more directly target the genes related to disease, but each has clear limitations. RNA-based therapies, such as mRNA and siRNA, face challenges with repeat dosing and related toxicities. Non-integrating viral gene therapy platforms, such as adeno-associated virus, or AAV, may have limited durability because they do not permanently change the genome and have limited efficacy upon re-administration due to resulting immune responses. Integrating viral gene therapy platforms, such as lentivirus, permanently alter the genome but do so randomly, which leads to the potential for undesirable mutations. Additionally, cells may recognize the transduced genes as foreign and respond by reducing their expression, limiting their efficacy. Thus, while our understanding of genetic diseases has increased tremendously since the mapping of the human genome, our ability to treat them effectively has been limited.

We believe gene editing has the potential to enable a next generation of therapeutics and provide curative solutions to many genetic diseases through precise gene modification. The process of gene editing involves precisely altering DNA sequences within the genomes of cells using enzymes to cut the DNA at specific locations. After a cut is made, natural cellular processes repair the DNA to either silence or correct undesirable

sequences, potentially reversing their negative effects. Importantly, because the genome itself is modified in this process, the change is permanent in the patient.

Earlier generation gene-editing technologies, such as zinc finger nucleases (ZFNs), transcriptor-activator like effector nucleases (TALENs) and meganucleases, rely on engineered protein-DNA interactions. While these systems were an important first step to demonstrate the potential of gene editing, their development has been challenging in practice due to the complexity of engineering protein-DNA interactions. In contrast, CRISPR/Cas9 is guided by RNA-DNA interactions, which are more predictable and straightforward to engineer and apply.

The CRISPR/Cas9 Technology

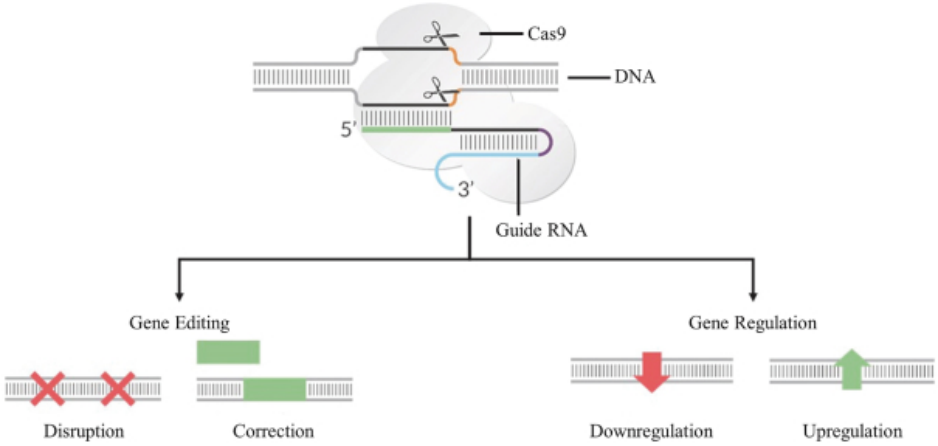
CRISPR/Cas9 evolved as a naturally occurring defense mechanism that protects bacteria against viral infections. Dr. Emmanuelle Charpentier and her collaborators elucidated this mechanism and developed ways to adapt and simplify it for use in gene editing. The CRISPR/Cas9 technology they described consists of three basic components: CRISPR-Associated protein 9, or Cas9, CRISPR RNA, or crRNA, and trans-activating CRISPR RNA, or tracrRNA. Cas9, in combination with these two RNA molecules, is described as “molecular scissors” that can make specific cuts in double-stranded DNA.

Dr. Emmanuelle Charpentier and her collaborators simplified the system for use in gene editing by combining the crRNA and tracrRNA into a single RNA molecule called a guide RNA. The guide RNA binds to Cas9 and can be programmed to direct the Cas9 enzyme to a specific DNA sequence based on Watson-Crick base pairing rules. The CRISPR/Cas9 technology can be used to make cuts in DNA at specific sites of targeted genes, providing a powerful tool for developing gene editing based therapeutics.

Once the DNA is cut, the cell uses naturally occurring DNA repair mechanisms to rejoin the cut ends. If a new DNA template with the correct sequence has been delivered to the cell prior to the time the DNA is cut, it will be incorporated, leading to a correction of the targeted gene, which we refer to as gene correction. Alternatively, if no DNA template is present, the cell will rejoin the two cut ends in a way that will likely lead to the disruption and inactivation of the gene, which we refer to as gene disruption.

CRISPR/Cas9 can also be adapted to regulate the activity of an existing gene without modifying the actual DNA sequence, which we refer to as gene regulation. This is accomplished using a catalytically inactive form of the Cas9 enzyme that can be directed to bind specific DNA sequences without cutting. By linking this inactive Cas9 to proteins that regulate gene function, the activity of specific genes can be either up or downregulated.

CRISPR/Cas9 gene editing

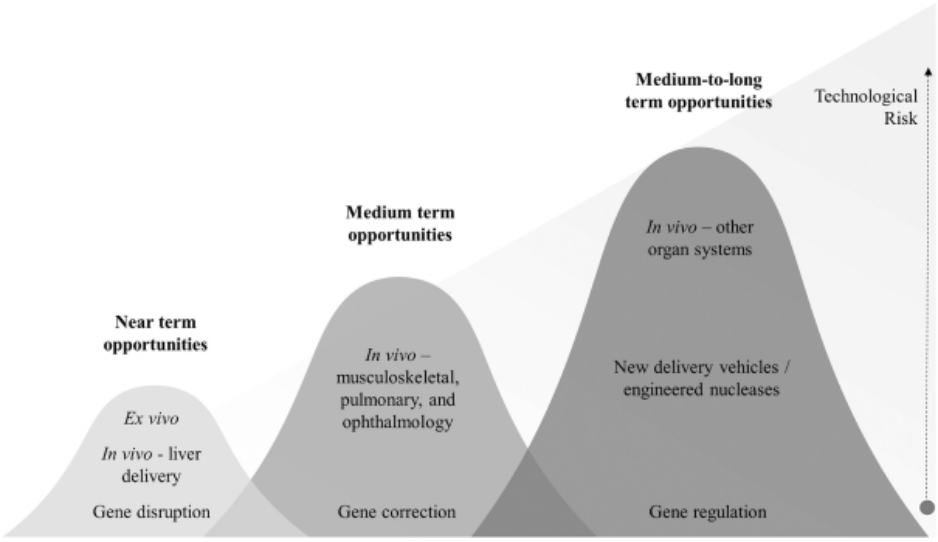


We believe that CRISPR/Cas9 is a versatile technology that can be used to either disrupt, correct or regulate genes. We intend to take advantage of the versatility and modularity of the CRISPR/Cas9 system to adapt and rapidly customize individual components for specific disease applications. Consequently, we believe that CRISPR/Cas9 may form the basis of a new class of therapeutics with the potential to treat a large number of both rare and common diseases.

Our Approach to CRISPR/Cas9 Portfolio Development

We have established a portfolio of programs by selecting disease targets based on a number of criteria, including high unmet medical need, advantages of CRISPR/Cas9 relative to alternative approaches, technical feasibility and the time required to advance the product candidate into and through clinical trials. For CRISPR/Cas9-based therapeutics, technical feasibility is primarily determined by the delivery modality and by the editing strategy required to treat the disease. The diagram below illustrates this spectrum of therapeutic applications, beginning with *ex vivo* delivery and gene disruption, progressing to *in vivo* organ systems and more sophisticated gene regulation strategies.

Strategic Progression of Our CRISPR/Cas9-Based Therapeutic Applications



We have initiated programs in three primary areas: (i) *ex vivo* programs involving gene editing of hematopoietic cells, (ii) *in vivo* programs targeting the liver and (iii) additional *in vivo* programs targeting other organ systems such as muscle and lung. By focusing our most advanced programs in *ex vivo* applications we believe we can mitigate technical and clinical risk, while also developing *in vivo* programs in parallel to fully realize the potential of our platform.

Strategic Partnerships and Collaborations

We intend to develop CRISPR/Cas9-based therapeutics both independently and in collaboration with current and potential future corporate partners. We have established collaborations with Bayer and Vertex which will provide over $400 million, inclusive of estimated spending on funded programs, which will be used to

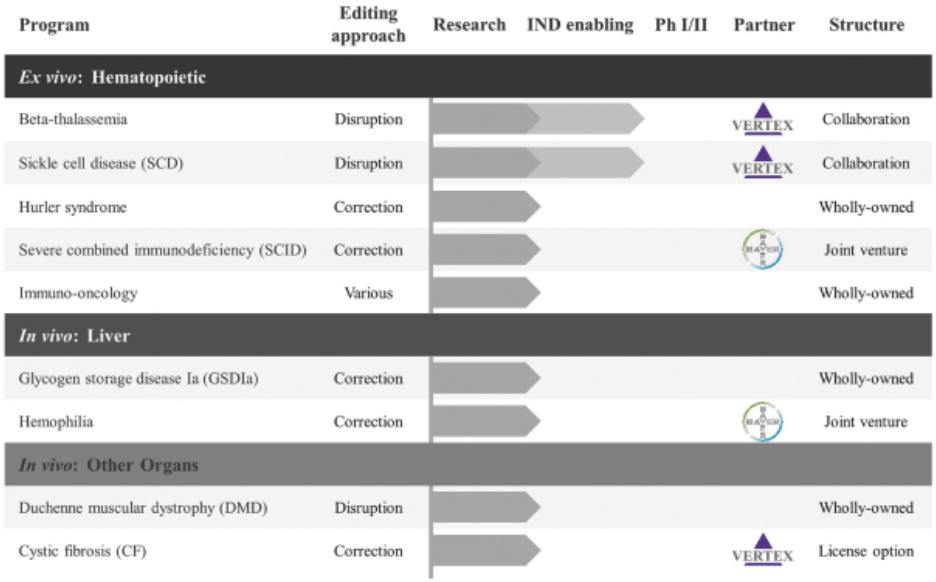
advance the programs included in these partnerships. These significant commitments will allow us to broaden our development portfolio, as well as invest in technology enhancements and delivery technologies. As part of these collaborations, Bayer and Vertex made equity investments of $35 million and $30 million, respectively, which we believe strengthen their commitments to the growth of our company. We believe that the resources committed by Bayer and Vertex illustrate the potential of our CRISPR/Cas9 gene editing technology.

Under our agreement with Bayer Healthcare, we established Casebia Therapeutics LLP, or Casebia, a joint venture in which we and Bayer Healthcare are equal owners. We intend for Casebia to largely focus on more challenging *in vivo* therapeutic areas in larger patient populations, and to invest resources in optimizing the platform and delivery technologies for *in vivo* delivery. Through our agreement, we will have access to technology enhancements developed or obtained by Casebia for the benefit of our other wholly owned programs.

Our agreement with Vertex is a two-part collaboration. We have retained co-development and co-commercialization rights for the hemoglobinopathies program. We have also granted Vertex an option to license certain programs, with the potential to receive milestone payments and royalties.

Our Pipeline

The following table summarizes the current status of our product development pipeline:



Ex Vivo *Hematopoietic Program*

Background

We are primarily utilizing *ex vivo* approaches to treat diseases related to the hematopoietic system, which is the system of organs and tissues, such as bone marrow, the spleen and lymph nodes, involved in the production of blood. Today, many of the hematopoietic system diseases we are targeting are treated with allogeneic hematopoietic stem cell transplants, or allo-HSCT. In performing allo-HSCT, physicians replace a patient's

blood-forming cells that contain the defective gene with cells obtained from a different person that contain the normal gene. Unfortunately, not all patients are able to be matched with suitable donors. Patients who do undergo allo-HSCT face a high risk of complications such as infections related to immunosuppression, transplant rejection and graft-versus-host disease, where immune cells in the transplanted tissue (the graft) recognize the recipient (the host) as "foreign" and begin to attack the host's cells.

In contrast to allo-HSCT, our approach harvests stem cells directly from the patient, edits the defective gene *ex vivo*, and reintroduces those same cells back into the patient. We believe this *ex vivo* gene editing approach, which uses the patient's own cells, will provide better safety and efficacy than allo-HSCT.

Our Lead Programs—Hemoglobinopathies

Our lead programs aim to develop a single, potentially transformative CRISPR/Cas9-based therapy to treat both beta-thalassemia and sickle cell disease, or SCD. These diseases are caused by specific mutations of the beta globin gene. Beta globin is an essential component of hemoglobin, a protein in red blood cells that delivers oxygen and removes carbon dioxide throughout the body. A number of factors make these attractive lead indications, including: (i) high unmet medical need, (ii) compelling market potential, (iii) well-understood genetics and (iv) the ability to employ an *ex vivo* gene disruption strategy.

Beta-thalassemia

Overview

Beta-thalassemia is a blood disorder that reduces the production of hemoglobin. This disease is caused by mutations that give rise to the insufficient expression of the beta globin protein, which can lead to symptoms related to not only the lack of hemoglobin, but also as result of the buildup of unpaired alpha globin proteins in red blood cells. The severity of symptoms associated with beta-thalassemia varies depending on the levels of functional beta globin present in the blood cells. In the most severe cases, described as beta-thalassemia major, functional beta globin is either completely absent or reduced, resulting in severe anemia. While chronic blood transfusions can be effective at addressing symptoms, they often lead to iron overload, progressive heart and liver failure, and eventually death. Patients with mild forms of beta-thalassemia may experience some mild anemia or even be asymptomatic.

The total worldwide incidence of beta-thalassemia is estimated to be 60,000 births annually, the total prevalence in the United States and the European Union is estimated to be 19,000 and there are over 200,000 people worldwide who are alive and registered as receiving treatment for the disease.

Limitations of current treatment options

The most common treatment for beta-thalassemia is chronic blood transfusions. Patients typically receive transfusions every two to four weeks and chronic administration of blood often leads to elevated levels of iron in the body and can cause organ damage over a relatively short period of time. Patients are often given iron chelators, or medicines to reduce iron levels in the blood, which are associated with their own significant toxicities. Low adherence to this burdensome regime often results in death by 30 years of age for patients with transfusion-dependent beta-thalassemia. The only potentially curative therapy for this disease is allo-HSCT, but few patients elect to have this procedure given its associated morbidity and mortality. In developing countries, where chronic transfusions are not available, most patients die in early childhood. We believe that our therapeutic approach could offer a potentially curative and safe treatment for this devastating disease.

Sickle Cell Disease

Overview

Sickle cell disease is an inherited disorder of red blood cells resulting from a mutation in the beta globin gene that causes abnormal red blood cell function. Under conditions of low oxygen concentration, the abnormal hemoglobin proteins aggregate within the red blood cells causing them to become sickled in shape and inflexible. These sickled cells obstruct blood vessels, restricting blood flow to organs, ultimately resulting in anemia, severe pain, infections, stroke, overall poor quality of life and early death.

The worldwide incidence of SCD is estimated to be 300,000 births annually and there are 20 million to 25 million people worldwide with the disease. In the United States, the total prevalence is estimated to be 100,000 individuals.

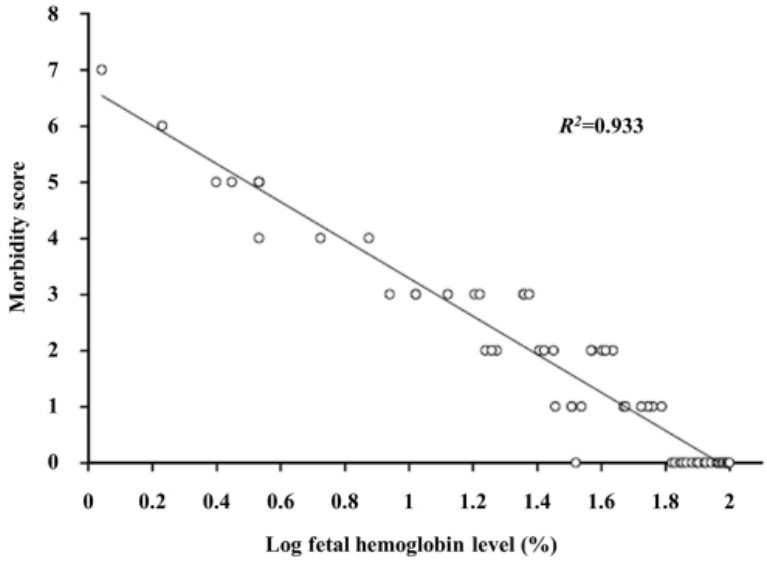
Limitations of current treatment options

As with beta-thalassemia, in regions where access to modern medical care is available, standard treatment for SCD involves chronic blood transfusions, which has the same associated risks of iron overload and toxicities associated with chelation therapy. Allo-HSCT is a second potential treatment option. While allo-HSCT provides the only potentially curative therapeutic path for SCD, it is often avoided given the significant risk of transplant-related morbidity and mortality in these patients.

Our Gene Editing Approach

Our therapeutic approach to treating beta-thalassemia and SCD employs gene editing to upregulate the expression of the gamma globin protein, a hemoglobin subunit that is commonly present only in newborn infants. Hemoglobin that contains gamma globin instead of beta globin protein is referred to as fetal hemoglobin, or HbF. In most individuals HbF disappears in infancy as gamma globin is replaced by beta globin through naturally occurring suppression of the gamma globin gene. The symptoms of beta-thalassemia and SCD typically do not manifest until several months after birth, when the levels of HbF have declined considerably. Some patients with beta-thalassemia or SCD have elevated levels of HbF that persist into adulthood, a condition known as hereditary persistence of fetal hemoglobin, or HPFH. Patients with HPFH are often asymptomatic, or experience much milder forms of disease. This protective HPFH condition has been shown to result from specific changes to the DNA in the cell, either in the region of the globin genes or in certain genetic regulatory elements that control the expression levels of the globin genes.

Relationship between level of HbF and morbidity in beta-thalassemia



We are using our CRISPR/Cas9 platform to mimic the same DNA sequence changes that occur naturally in HPFH patients. We plan to isolate patients' hematopoietic stem cells, which differentiate into red blood cells, treat these cells *ex vivo* with a CRISPR/Cas9 therapeutic to edit their DNA to upregulate the expression of the gamma globin protein and reintroduce the edited cells back into the patients. We believe that the genetically modified stem cells will give rise to red blood cells that contain HbF and significantly reduce the severity of the symptoms associated with these two diseases.

An alternative CRISPR/Cas9 approach to treating hemoglobinopathies would be to correct the mutated beta globin gene. We have chosen the HbF upregulation strategy given the relative technical simplicity of the gene deletion strategy involved, ability of this strategy to counteract a wide variety of different beta globin mutations, and the absence of symptoms in patients with high HbF levels.

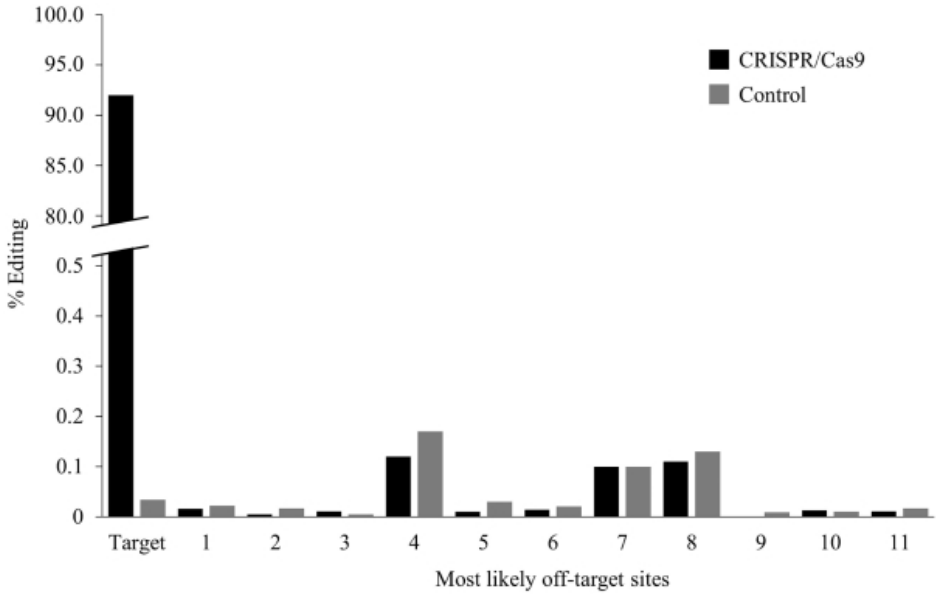
Our CRISPR/Cas9 gene editing strategy has significant advantages over other gene therapies in development for the treatment of hemoglobinopathies. For example, lentivirus-based treatments involve a random integration of one or more copies of the globin gene throughout the genome. The expression levels of the newly introduced gene can vary depending on the exact location of the DNA in the genome, leading to inconsistent and variable levels of expression. In addition, with each random integration, a mutation may be created, which may have an associated safety concern, including the potential to cause cancer.

Preclinical Data

We are progressing toward initiating clinical trials for our hemoglobinopathy programs. The first step in this process involves selecting the specific gene editing strategy and RNA guides we will use in our therapeutics. We are applying our high-throughput target evaluation process to test a number of these approaches, and ultimately select RNA guides with the highest editing rate of the globin genes and the greatest effect on HbF expression. Using our high-throughput guide screening platform, we have been able to identify guide RNAs that allow editing of hematopoietic stem cells at specific locations in the genome with greater than 90% efficiency.

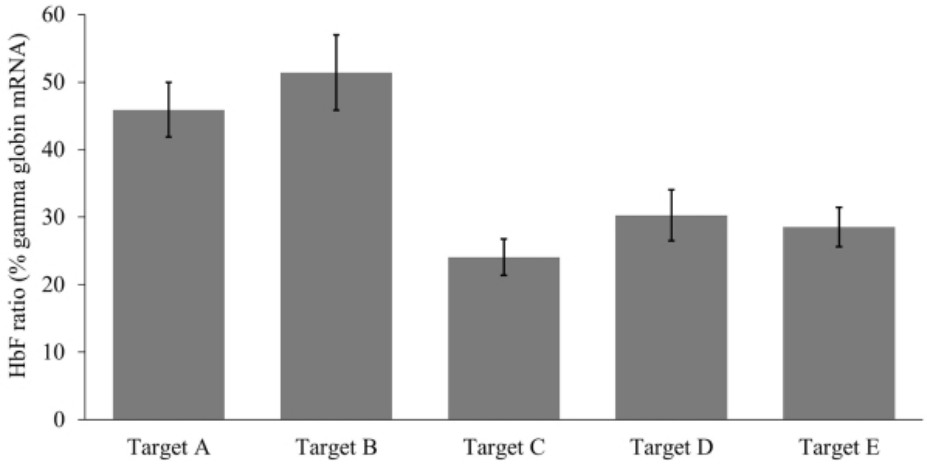
In addition to selecting guide RNAs with the highest cutting activity, we also screen our guide RNAs for off-target effects, or the introduction of cuts in DNA at locations other than the target sequence. To do this, we use bioinformatics to predict the most likely sites of off-target cuts, then test for cuts at these locations. The example guide RNA analysis shown below illustrates that we are able to identify guide RNAs that cut very efficiently at the target sites but show no off-target activity above control levels, even at sites where off-target activity is most likely to occur. We also test our lead candidates for any unlikely off-target effects using genome sequencing before advancing them for use as therapeutics.

Example guide RNA analysis



There are multiple naturally occurring genetic variants that lead to HPFH and which could form the basis of our therapeutic. We have used CRISPR/Cas9 to recreate a number of these variants and tested their ability to upregulate HbF. The figure below shows the level of HbF upregulation resulting from the recreation from five different genetic variants in hematopoietic stem cells using CRISPR/Cas9. We believe that at least two of these, named “Target A” and “Target B”, may result in potentially curative levels of HbF if successfully introduced to patients with beta-thalassemia and SCD.

Ability of different gene targets to drive HbF production



To date, we have identified guide RNAs that perform the desired gene edits with very high efficiency, result in high levels of HbF production in cells and show no detectable evidence of off-target effects. As we continue to advance our hemoglobinopathies programs to the clinic, we are in the process of evaluating the ability of edited hematopoietic stem cells to engraft and persist in mice. Before entering clinical trials we will also perform longer-term studies in mice to ensure there are no undesirable consequences caused by the gene edited cells.

Hurler Syndrome

Hurler syndrome is a type of mucopolysaccharide disease caused by a defective IDUA gene. The IDUA gene is responsible for encoding alpha-L-iduronidase, an enzyme that breaks down large molecules called glycosaminoglycans, or GAGs, in the lysosomes of cells. A defective IDUA gene results in a lack of alpha-L-iduroindase which leads to an accumulation of GAGs and results in cellular dysfunction and severe clinical abnormalities. Patients with Hurler syndrome have a broad spectrum of clinical problems including skeletal abnormalities, enlarged livers and spleens, and severe intellectual disability due to a lack of this enzyme in the brain. Most patients experience a decline in intellectual development and often lose both vision and hearing as the disease progresses. Without treatment, the average age at death is five years, and nearly all patients die by the age of ten. The worldwide incidence of Hurler syndrome is approximately one in 100,000 births.

There are two common approaches to treating mucopolysaccharide diseases: enzyme replacement therapy and allo-HSCT. Enzyme replacement therapy, or ERT, does not adequately address the symptoms of Hurler syndrome because it cannot cross the blood-brain barrier to address the severe neurologic symptoms associated

with this disease. While allo-HSCT can be effective in treating the disease, it is associated with significant morbidity and mortality, and not all patients are able to find suitable donors. Even when a match is found, the delay between diagnosis and treatment often results in significant irreversible disease progression. Our approach is to introduce a functional copy of the IDUA gene into a patient's own hematopoietic cells using *ex vivo* CRISPR/Cas9 gene editing, before returning them to the patient. We believe that using a patient's own cells rather than those from a donor will eliminate a potentially lengthy search for an appropriate donor, allowing us to intervene at an earlier point and avoid the significant risks associated with allo-HSCT.

Severe Combined Immunodeficiency Disease

Severe combined immunodeficiency disease, or SCID, is a disease in which the patient's immune system is compromised and cannot fight off infections. These patients are identified early in life because they often suffer from recurrent severe respiratory infections, which can be life-threatening in the absence of a functioning immune system. There are multiple underlying causes of SCID, and in one particularly severe form, a gene called RAG1 is mutated. Mutations in RAG1, a gene that plays a critical role in the process of antibody generation, prevent normal development of the patient's immune system, resulting in an absence of B-cells, a type of white blood cell. The worldwide incidence of SCID is estimated to be one in 58,000 births, with the RAG1 mutation associated form accounting for approximately 15% of patients.

Currently, the only curative therapy for this potentially fatal disorder is allo-HSCT, which carries a high risk of complications. Gene therapies for SCID insert copies of a replacement gene randomly into the genome, potentially resulting in unwanted mutations. The risks associated with this type of gene therapy were underscored in a clinical trial for another variant of SCID in which five out of twenty patients developed leukemia. We believe that the precise correction of the RAG1 gene with CRISPR/Cas9 will bring benefit to these patients while minimizing the risk of leukemia associated with gene therapy. Considering corrected cells proliferate faster than non-corrected cells, we believe that a small number of corrected cells reintroduced into the patient could provide a therapeutic benefit and in time, compensate for the defective cells. With our *ex vivo* approach, we believe we can attain sufficient levels of correction to generate the desired therapeutic benefit. Our Casebia joint venture with Bayer Healthcare will lead development of our SCID program, and leverage Bayer Healthcare's expertise in hematologic disorders.

Future Development Opportunities

Engineered Cell Therapies For Cancer Immunotherapy

Over the past several years, interest in the oncology community has centered on immunotherapy, or treatments that harness a patient's own immune system to attack cancer cells. Engineered cell therapy is one such immunotherapy approach, in which immune system cells such as T-cells and natural killer, or NK, cells are genetically modified to enable them to recognize and attack tumor cells.

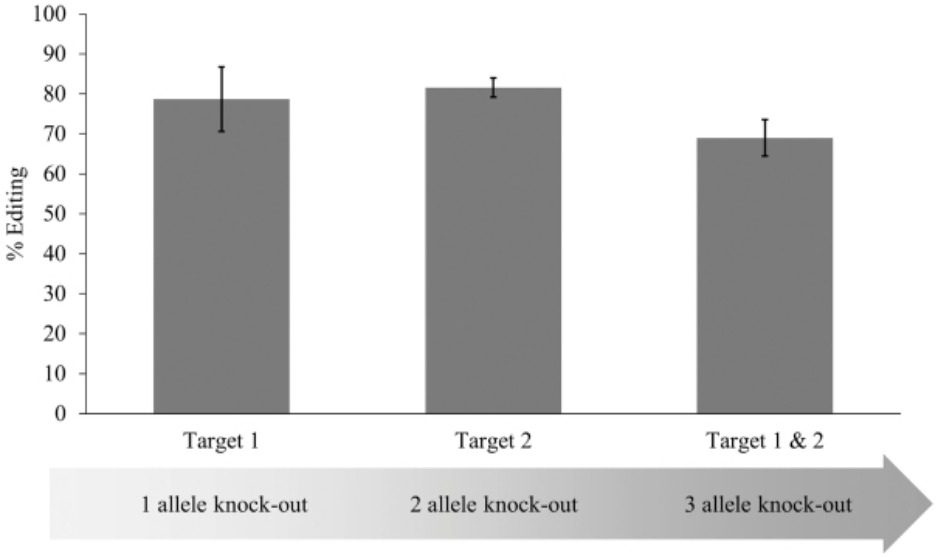
Engineered cell therapy has demonstrated encouraging clinical results and shown the potential to become an entirely new class of oncology therapeutics; however, realizing this full potential will require overcoming some key challenges. Most engineered cell therapies in development require unique products to be created for each patient treated, using conventional techniques. This approach to drug development is both inefficient and cost-prohibitive. Additionally, these versions of engineered cell therapies appear limited in their ability to treat solid tumors. These products have also demonstrated sub-optimal safety profiles, including overstimulation of the immune system, occasionally resulting in death.

We are utilizing CRISPR/Cas9 to create an "off-the-shelf" cell therapy, overcoming the inefficiency and cost of creating a unique product for each patient. In addition to delivering a gene for an engineered receptor to target the tumor, creating such a product would require simultaneous disruption of several genes in order to prevent off-target immune responses. We have initial results demonstrating that this type of "multiplexed"

editing can be achieved with high efficiency using CRISPR/Cas9. We are also using our platform to make other improvements such as disruption checkpoint inhibitor genes to overcome solid tumor suppression, and disrupting other genes to improve the safety profile.

We expect that the cellular engineering strategies that are ultimately successful in cancer immunotherapy will involve multiple genetic modifications, an application for which we believe CRISPR/Cas9 will play a central role. While other gene editing platforms could potentially be used for these purposes, CRISPR/Cas9 is particularly well-suited for multiplexed editing. Current gene editing techniques that require different protein enzymes for each genetic modification may be limited in the number of edits they can make concurrently. In contrast, CRISPR/Cas9 can make multiple edits using a single Cas9 protein and multiple small guide RNA molecules with high efficiency, as shown below.

Multiplexed editing of human primary T-cells using CRISPR/Cas9



In Vivo Programs

In parallel with our *ex vivo* programs, we are pursuing a number of *in vivo* indications which will involve delivery of CRISPR/Cas9 therapeutics directly to tissues within the human body. Our initial *in vivo* applications will target the liver, leveraging well-established delivery technologies. We have also begun optimizing delivery systems to target other organ systems, including musculoskeletal and pulmonary.

Liver Diseases

We have selected liver diseases as our initial *in vivo* targets because delivery of nucleic acid therapies into the liver has been clinically established and validated delivery technologies are now available, including, but not limited to, lipid nanoparticle based delivery vehicles, or LNPs, and AAVs. We believe this proof of concept reduces the challenges associated with delivering CRISPR/Cas9-based therapeutics *in vivo* to the liver.

Within the liver we are pursuing diseases that have well understood genetic linkages, and have begun preclinical development for multiple indications including glycogen storage disease Ia, or GSDIa, and hemophilia. In both of these indications, evidence suggests that correction of the mutant gene in only a small percentage of liver cells may have a significant therapeutic effect, which makes the gene correction strategy feasible in these indications.

Glycogen Storage Disease Ia

Overview

GSDIa, also known as Von Gierke disease, is an autosomal recessive inborn error of glucose metabolism caused by a mutation in the G6PC gene, which encodes the glucose-6-phosphatase protein, or G6Pase. In patients with GSDIa, the lack of G6Pase prevents the release of glucose from the liver, resulting in accumulation of a large chain form of glucose known as glycogen. The inability of patients with GSDIa to regulate glucose levels leads to hypoglycemia, or low blood glucose, and high levels of lactic acid when patients are not eating, requiring patients to adhere to burdensome dietary regimes. GSDIa patients also face long-term risks such as growth delay, neuropathy and kidney stones. Additionally, due to the accumulation of glycogen in the liver, 70% to 80% of patients over 25 years of age will develop hepatocellular adenomas, a type of non-cancerous growth in the liver, of which approximately 10% will progress to hepatocellular carcinoma, a potentially fatal liver cancer. There are approximately 1,000 new cases of GSDIa per year worldwide.

Limitations of Current Treatment Options

There are currently no disease-modifying treatment options for patients with GSDIa. Any disruption in carbohydrate delivery may lead to low blood sugar levels, which can cause life-threatening consequences including seizure, coma and death. To minimize the risk of acute complications, patients are required to adhere to highly burdensome, life long dietary regimens such as overnight administration of uncooked cornstarch or a slow-release carbohydrate product such as Glycosade. These regimens have a high rate of non-compliance, leading to increased risk of serious long-term complications.

Our Gene Editing Approach

We are developing a CRISPR/Cas9 therapy to correct the mutation in GSDIa patients. Animal model experiments have demonstrated that the addition of functional copies of the G6PC gene is capable of correcting the deficiency of G6Pase protein in GSDIa and that as little as 3% of normal levels of G6Pase can restore the equilibrium of glucose and glycogen in the bloodstream and liver. Our approach is to correct the G6PC gene directly in its native location. We believe this direct gene correction will result in appropriate expression of the G6Pase protein. Other methods rely on adding copies of the gene through viral delivery methods, which we believe may lead to overexpression of the G6Pase protein and ineffective control of glucose levels.

Hemophilia

Overview

Hemophilia is an X-linked recessive genetic disease primarily present in male children. Our initial hemophilia program targets hemophilia B, which results from a deficiency in factor IX, an enzyme produced in the liver. Factor IX is part of the blood coagulation system, which enables blood to form clots in response to injury and bleeding. A lack of factor IX leads to an increased risk of bleeding, either spontaneously or in response to injury.

Patients with severe forms of the disease are first diagnosed at infancy, as witnessed through prolonged bleeding from simple medical procedures or through excessive bruising from simple falls. These patients have frequent spontaneous bleeding into joints and muscles, which can lead to edema, inflammation and debilitating

pain. Patients with mild forms of the disease typically present as normal, and diagnosis usually follows surgery or trauma. The worldwide prevalence of hemophilia B patients is estimated to be 28,000, including over 4,000 in the United States. About half of hemophilia B cases are classified as severe based on levels of factor IX activity that are less than 1% of normal.

Limitations of Current Treatment Options

The standard of care for symptomatic patients with hemophilia B involves enzyme replacement with recombinant factor IX. Exogenous factor IX protein is administered both as a prophylaxis and during acute bleeding episodes. While considered effective, factor IX replacement therapies are invasive, inconvenient and non-curative. Until recently, hemophilia B therapy required weekly intravenous injections or infusions. While administration frequency has improved in recent years, key drawbacks of protein therapy, including fluctuations in factor IX levels, remain a significant pitfall of enzyme replacement therapies.

Our Gene Editing Approach

We believe that hemophilia B symptoms can be dramatically reduced with only a moderate restoration in factor IX activity. It has been shown that patients with more than 5% of normal factor IX activity have milder forms of the disease and may not present symptoms in the absence of trauma or surgery. This observation implies that in patients with severe forms of the disease, restoration of factor IX activity to a level of 5% or more of normal may be clinically meaningful.

The correction of a mutant factor IX gene with CRISPR/Cas9 leverages endogenous regulation via correction of the gene at its native location within the genome. As a result, we believe it represents a superior way to treat hemophilia B patients, relative to other gene therapy approaches that insert the correct gene at a random location in the genome. Our hemophilia program will be developed within the Casebia joint venture, leveraging Bayer's expertise in this disease area together with our gene editing expertise.

Other Organs

We intend to pursue select *in vivo* programs targeting diseases of other organ systems such as Duchenne muscular dystrophy, or DMD, and cystic fibrosis, which have significant patient populations with high unmet medical needs, and we believe are well suited for a CRISPR/Cas9 gene editing system. For cystic fibrosis, or CF, we are working with Vertex, a global leader with extensive disease area expertise. We are working internally as well as through third-party collaborations to optimize viral and non-viral delivery technologies to overcome the delivery challenges to these organ systems.

Duchenne Muscular Dystrophy

Overview

Duchenne muscular dystrophy is an X-linked recessive genetic disease caused by a mutation in the dystrophin gene, which results in a lack of the dystrophin protein, a protein that plays a key structural role in muscle fiber function. The absence of dystrophin in muscle cells leads to significant cell damage and ultimately causes muscle cell death and fibrosis. DMD is characterized by muscle degeneration, loss of mobility and premature death, and is among the most prevalent severe genetic diseases, occurring in one in 3,300 male births worldwide. There is also a related form of muscular dystrophy called Becker muscular dystrophy, or BMD, which is also caused by mutations in the dystrophin gene. However, unlike DMD, the mutations in BMD result in the loss of certain exons or regions of the gene, and can lead to an abnormal version of dystrophin that retains some function. As a result, BMD patients have milder symptoms than DMD patients.

There are currently no approved disease-modifying therapies in the United States for the treatment of either DMD or BMD. Our gene-based therapeutic approach in development to treat DMD involves the use of

oligonucleotides to promote exon skipping over the mutations that otherwise would result in truncated dystrophin synthesis. While exon skipping has demonstrated promising results in limited settings, larger clinical trials of this approach have suggested only modest efficacy. In addition, delivering sufficient levels of oligonucleotides requires repeated administration and presents challenges to treating DMD.

Our Gene Editing Approach

We are pursuing multiple approaches to developing therapies for DMD. Our first approach is to deliver CRISPR/Cas9 directly to muscle cells in patients to delete the defective exons in the dystrophin gene. The goal of this approach is to allow the gene to regain some functional capacity and produce enough dystrophin protein to diminish the more severe symptoms of DMD to resemble the milder form of the disease known as BMD. We believe that currently available technology is capable of delivering the CRISPR/Cas9 into muscle cells, and together with the relatively high efficiency of exon deletion using the CRISPR/Cas9 system, we will be able to move this program into clinical testing.

Another approach we are exploring is cell therapy in an *ex vivo* setting. We will attempt to isolate muscle precursor cells, or satellite cells, from healthy donors and modify them *ex vivo* using our CRISPR/Cas9 technology to disrupt the genes that cause cell rejection. Once administered to the patient, we believe that the cells will divide and provide the patient with properly functioning copies of the dystrophin gene.

In parallel, we are performing *in vitro* experiments to test the principle of dystrophin gene correction which could potentially be curative. Prior studies in mice and humans have indicated that dystrophin levels as low as 4 to 15% of normal are sufficient to ameliorate symptoms, suggesting that even a partial restoration of dystrophin levels would be therapeutically beneficial.

Cystic Fibrosis

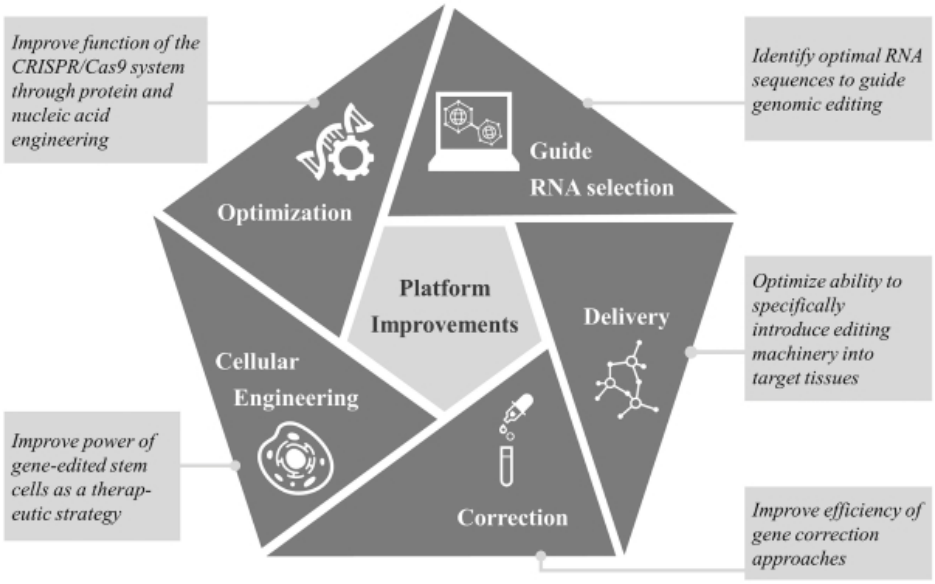
Cystic fibrosis is a progressive disease caused by mutations in the cystic fibrosis transmembrane regulator, or CFTR, gene resulting in the loss or reduced function of the CFTR protein. Although there are several different mutations associated with CF, approximately 70% of CF patients have the same mutation at codon 508 of the CFTR gene. Patients with CF develop thick mucus in vital organs, particularly in the lungs, pancreas and gastrointestinal tract. As a result, CF patients experience chronic severe respiratory infections, chronic lung inflammation, poor absorption of nutrients, progressive respiratory failure and early mortality.

CF is an orphan disease that affects an estimated 70,000 to 100,000 patients worldwide, with a majority in the United States and Europe. The median age of death from CF in the United States in 2014 was 29 years, with most deaths resulting from respiratory failure. CF patients require lifelong treatment with multiple daily medications and hours of self-care. They often require frequent hospitalizations and sometimes even lung transplantation, which can prolong survival but is not curative.

Studies have shown that as little as 10% of normal CFTR function can ameliorate disease symptoms. Our approach is focused on using our CRISPR/Cas9 technology to correct the mutation at codon 508. Together with our collaboration partner Vertex, we believe that we will be able to deliver CRISPR/Cas9 to the lung and correct this mutation sufficiently to improve symptoms in patients with CF.

Further Unlocking the Potential of Our CRISPR/Cas9 Platform

We are working to optimize our CRISPR/Cas9 platform. Our key areas of focus are described below.



Optimization of the Cas9 Protein

The Cas9 nucleases found in nature are highly efficient and specific. We believe that for many gene-editing applications, the naturally occurring Cas9 variants have all the properties required to support an effective therapeutic. However, we also see potential in certain disease areas and organ systems where modified versions of Cas9 may be more effective, and we are working internally and through our external collaborations to develop these.

Our research and development efforts seek to enhance a number of characteristics of Cas9, including size, specificity, immunogenecity and ability to support different types of editing strategies. We believe that the process of optimizing these different parameters may yield a number of effective Cas9 versions with different properties, each of which may be best suited to a certain disease area or type of genetic editing.

Guide RNA Selection

Selecting the sequence for guide RNAs is a critical step in the process of designing our therapeutics. Once we have chosen a gene editing strategy, we seek to identify guide RNAs that will perform the desired edit with high efficiency and with extremely low off-target cutting. While computational models can predict efficiency and off-target effects with reasonable accuracy, we believe that a combination of computation and experimental approaches is necessary to reliably select the best possible guide RNAs.

We are building a guide RNA selection process that combines bioinformatics and experimental assays to enable the screening of over 10,000 guide RNAs in each experiment. This process starts with proprietary bioinformatics algorithms that select a large pool of guide RNAs that are predicted to have desired properties.

These guides are then tested for target site cutting efficiency using a high-throughput screening platform in a model cell line. The most efficient guides are then put through two screening processes for possible off-target effects. First, bioinformatics algorithms are used to identify the 10 to 20 sites in the genome that are most likely to show off-target effects, and these sites are examined through high-throughput assays for empirical off-target cutting. Second, whole genome sequencing is performed to identify any potential off-target cutting, even at unpredicted locations. Finally, a small subset of guides with the highest efficiency and lowest off-target potential are tested in the cell type of therapeutic interest before choosing a lead guide or guides for our program.

Delivery

Delivery of CRISPR/Cas9 into cells is a critical step to ensure that the therapeutic will be effective. We can deliver our Cas9 in the form of protein, DNA or RNA, allowing us to tailor the delivery format to the target tissue. For our *ex vivo* programs, we are using both protein and mRNA forms of Cas9 delivered via electroporation. For *in vivo* delivery to cells and organs in the patient we are evaluating a range of technologies that include LNPs and AAVs as well as other delivery methods.

We have access to leading expertise and technology for LNPs through our advisory relationship with Dr. Daniel Anderson at Massachusetts Institute of Technology. We are currently testing a variety of LNP and AAV technologies which are available from a variety of sources, before selecting the specific versions for use in our therapeutics. In addition, we are collaborating externally to develop next-generation delivery technologies that will allow us to access organ systems that are less accessible today. Some of this activity may be done through our Casebia joint venture with Bayer which provides us access to supporting technologies such as delivery vehicles.

Correction

While gene correction is achievable today using CRISPR/Cas9, it is more difficult and has lower efficacy than the more straightforward gene disruption strategy. Our initial gene correction programs target diseases in which therapeutic efficacy can be achieved through correction of only a small percentage of cells, while other potential indications may require correction of a significantly higher percentage of cells. We are working with our collaborators to increase the efficiency of gene correction in order to facilitate the potential treatment of these additional indications.

A central focus of our development efforts is to optimize the correction rates in cell types where rates of correction are typically low. Some of this optimization is being done internally, to test the influence of different parameters of the CRISPR/Cas9 system on correction efficiency. In addition, we are advised by Dr. Stephen Elledge, Professor of Genetics at Harvard Medical School, who is an expert in DNA damage and repair, to explore ways to optimize the cellular processes involved in the correction process. We are also collaborating more broadly with leaders in the DNA repair field, to explore other approaches to optimize correction rates.

Cellular Engineering

Many *ex vivo* applications of our technology use a strategy of editing stem cells *ex vivo* which, when returned to the patient, differentiate into a variety of different cell types. For certain stem cell types, especially hematopoietic cells, there are well-established procedures to support this strategy. For others, these procedures are more nascent and require further development. A critical focus for us is to improve the efficacy, efficiency and safety of the *ex vivo* cell collection, manipulation and administration process for a variety of stem cell types. We are evaluating technologies to improve mobilization of a patient's stem cells, to maintain viability of the harvested cells, and to improve the ability of these cells to engraft into a patient's body. Both in our own laboratories and through our academic partnerships, we intend to perform additional research to optimize these parameters for each organ system.

Intellectual Property

We strive to protect and enhance the proprietary technologies that we believe are important to our business by seeking patents to cover our platform technology and its therapeutic uses. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for our technology, our ability to defend and enforce our intellectual property rights and our ability to operate without infringing any valid and enforceable patents and proprietary rights of third parties.

In-Licensed Intellectual Property

In April 2014, we exclusively licensed certain of Dr. Emmanuelle Charpentier's rights to a family of patent applications relating to CRISPR/TRACR/Cas9 complexes and their use in targeting or cutting DNA. Our license from Dr. Charpentier is limited to therapeutic products such as pharmaceuticals and biologics and any associated companion diagnostics, for the treatment or prevention of human diseases, disorders, or conditions. For further information about our license from Dr. Charpentier, please see "Business – CRISPR License with Dr. Emmanuelle Charpentier."

This family of patent applications includes a granted patent in the United Kingdom and pending patent applications in the United States, Europe, Canada, Mexico, Australia and other selected countries in Central America, South America, Asia and Africa. The granted patent in the United Kingdom and any other patents that may ultimately issue in this patent family are expected to expire in 2033, not including any applicable extensions.

In addition to Dr. Emmanuelle Charpentier, this family of patent applications has named inventors who assigned their rights either to California or Vienna. California's rights are subject to certain overriding obligations to the sponsors of its research, including the Howard Hughes Medical Institute and the U.S. Government. Caribou Biosciences, or Caribou, has reported that it has an exclusive license to patent rights from California and Vienna, subject to a retained right to allow non-profit entities to use the inventions for research and educational purposes. Intellia Therapeutics has reported that it has an exclusive license to such rights from Caribou in certain fields. For further information regarding the effects of joint ownership in the United States and abroad, please see "Risk Factors – Certain of our in-licensed intellectual property is jointly owned, and our license is from only one of the joint owners, materially limiting our rights in the United States and abroad."

In January 2016, the U.S. Patent and Trademark Office, or USPTO, declared an interference between one of the pending U.S. patent applications in this family and twelve issued U.S. patents and one U.S. patent application owned jointly by the Broad Institute and Massachusetts Institute of Technology and, in some instances, the President and Fellows of Harvard College, which we refer to individually and collectively as Broad. An interference is a proceeding conducted at the USPTO by the Patent Trial and Appeal Board, or PTAB, to determine which party was the first to invent subject matter claimed by at least two parties. There are currently two parties to this interference. The USPTO designated Dr. Emmanuelle Charpentier, California and Vienna collectively as "Senior Party" and designated Broad as "Junior Party." Following motions by the parties and other procedural matters, the PTAB could conclude that the contested subject matter is not patentable to the Senior Party, which in this case could preclude Senior Party's U.S. patent application from issuing as a patent; that the contested subject matter is not patentable to the Junior Party, which in this case could result in the cancellation of some or all of the Junior Party's claims; that the contested subject matter is not patentable to either party; or that the interference should be dismissed. Either party can appeal an adverse decision to the U.S. Court of Appeals for the Federal Circuit. For further information regarding risks regarding the interference and patent rights held by third parties, please see "Risk Factors—Risks Related to Our Intellectual Property."

CRISPR-Owned Intellectual Property

We also own 16 families of patent applications relating to our platform technology or its therapeutic applications. These patent applications are currently pending in the United States and in some cases in foreign

countries, and we may elect to pursue additional related applications in foreign countries. Any patents that ultimately issue from these patent applications may begin to expire in 2036.

Patent Assignment Agreement

In November 2014, we entered into a patent assignment agreement with Dr. Emmanuelle Charpentier, Dr. Ines Fonfara and the University of Vienna, or the Patent Assignment Agreement. Under the Patent Assignment Agreement, Dr. Charpentier, Dr. Fonfara and the University of Vienna assigned to us all rights to a family of patent applications relating to certain additional CRISPR/TRACR/Cas9 complexes and their use in targeting or cutting DNA.

As consideration for the patent rights assigned to us, we agreed to pay an upfront payment, milestone payments beginning with the filing of a U.S. Investigational New Drug application or its equivalent in a foreign country, a minimum annual royalty, a low single-digit royalty on net sales of products whose manufacture, use, sale, or importation is covered by the assigned patent rights, and a low single-digit percentage of licensing revenues.

We are obliged to use commercially reasonable efforts to obtain regulatory approval to market a product whose manufacture, use, sale, or importation is covered by the assigned patent rights, including but not limited to an obligation to use commercially reasonable efforts to file a U.S. Investigational New Drug application (or its equivalent in a major market country) by November 2021.

License Agreements

CRISPR License With Dr. Emmanuelle Charpentier

In April 2014, we entered into a license agreement, or the Charpentier License Agreement, with Dr. Emmanuelle Charpentier, one of our co-founders, pursuant to which we received an exclusive license under Dr. Charpentier's joint ownership interest a family of patent applications relating to CRISPR/TRACR/Cas9 complexes and their use in targeting or cutting DNA, which we refer to as the Patent Rights, to research, develop and commercialize therapeutic products such as pharmaceuticals or biological preparations, and any associated companion diagnostics, for the treatment or prevention of human diseases, disorders, or conditions, other than hemoglobinopathies, which we refer to as the CRISPR Field. The license is exclusive, even as to Dr. Charpentier, except that she retains a non-transferable right to use the technology for her own research purposes and in research collaborations with academic and non-profit partners. Additionally, the Charpentier License granted us an exclusive, worldwide, royalty-free sublicense, including the right to sublicense, to research, develop, produce, commercialize and sell therapeutic products relating to the CRISPR Field which incorporate any intellectual property that TRACR Hematology Ltd., our majority-owned subsidiary, or TRACR, develops under its license with Dr. Charpentier. In turn, we granted to Dr. Charpentier an exclusive license with the obligation to sublicense to TRACR any intellectual property we develop under the license with Dr. Charpentier for treatment and prevention of hemoglobinopathy in humans, including, without limitation, sickle cell disease and thalassemia.

Under the terms of the Charpentier License Agreement, as consideration for the license, Dr. Emmanuelle Charpentier received a technology transfer fee, an immaterial annual maintenance fee, immaterial milestone payments that will be due after the initiation of clinical trials, a low single digit percentage royalty on net sales of licensed products, and a low single digit percentage royalties of sublicensing revenue. We are obligated to use commercially reasonable efforts to obtain regulatory approval to market a licensed therapeutic product. CRISPR must use commercially reasonable efforts to file a U.S. Investigational New Drug application (or its equivalent in a major market country for a therapeutic product in the CRISPR field) by April 2021. In addition, CRISPR must file a U.S. Investigational New Drug application (or its equivalent in a major market country) for a therapeutic product in the CRISPR field by April 2024.

Unless terminated earlier, the term of the Charpentier License Agreement will expire on a country-by-country basis, upon the expiration of the last to expire valid claim of the Patent Rights in such country. We have the right to terminate the agreement at will upon 60 days' written notice to Dr. Emmanuelle Charpentier. We and Dr. Charpentier may terminate the agreement upon 90 days' notice in the event of a material breach by the other party, which is not cured during the 90 day notice period. Dr. Charpentier may terminate the license agreement immediately if we challenge the enforceability, validity, or scope of any Patent Rights.

TRACR License With Dr. Emmanuelle Charpentier

In April 2014, concurrently with our license agreement with Dr. Emmanuelle Charpentier, TRACR Hematology Ltd., our majority owned subsidiary, entered into a license agreement, or the TRACR License Agreement, with Dr. Charpentier, a minority shareholder of TRACR, under the Patent Rights. Pursuant to the TRACR License Agreement, TRACR is granted an exclusive, worldwide, royalty-bearing license, including the right to sublicense, to research, develop, produce, commercialize and sell therapeutic and diagnostic products for the treatment and prevention of hemoglobinopathy in humans, including sickle cell disease and thalassemia, or the TRACR Field. TRACR also receives a non-exclusive, worldwide, royalty-free license, including the right to sublicense, to carry out internal pharmaceutical research for therapeutic products outside of the TRACR Field and an exclusive, worldwide, royalty-free sublicense, including the right to sublicense, to research, develop, produce, commercialize and sell therapeutic products relating to the TRACR Field which incorporate any intellectual property that CRISPR develops under its license with Dr. Charpentier. In turn, TRACR grants to Dr. Charpentier an exclusive license to sublicense to CRISPR any intellectual property that TRACR develops under the license with Dr. Charpentier for use in the CRISPR Field.

TRACR is obligated to use commercially reasonable efforts to research, develop, and commercialize at least one therapeutic products for the prevention or treatment of human disease under the license agreement. TRACR must use commercially reasonable efforts to file a U.S. Investigational New Drug application (or its equivalent in a major market country for a therapeutic product in the TRACR field by April 2021. In addition, TRACR must file a U.S. Investigational New Drug application (or its equivalent in a major market country) for a therapeutic product in the TRACR field by April 2024. Tracr is solely responsible for all clinical, regulatory and development costs.

Under the TRACR License Agreement, Dr. Emmanuelle Charpentier is entitled to receive immaterial clinical and regulatory milestone payments per product that TRACR commercializes. TRACR is also required to pay Dr. Charpentier low single digit percentage royalties on the net sales of any approved therapeutic or diagnostic products, made by it, its affiliates, or its sublicensees and low single-digit percentage royalties on sublicensing revenue.

Unless terminated earlier, the term of the license agreement will expire on a country-by-country basis, upon the expiration of the last to expire valid claim of the Patent Rights in such country. TRACR has the right to terminate the agreement at will upon 60 days' written notice to Dr. Emmanuelle Charpentier. TRACR and Dr. Charpentier may terminate the agreement upon 90 days' notice in the event of a material breach by the other party, which is not cured during the 90 day notice period. Dr. Charpentier may terminate the license agreement immediately if TRACR challenges the enforceability, validity, or scope of any Patent Right.

Bayer Joint Venture

In December 2015, we entered into a Joint Venture Agreement, or the JV Agreement, with Bayer HealthCare LLC, or Bayer Healthcare, to create Casebia Therapeutics LLP, or Casebia, to discover, develop and commercialize new therapeutics for genetically linked diseases, including blood disorders, blindness and congenital heart disease. At the closing of the transactions contemplated by the JV Agreement in March, 2016, or the Closing, we contributed $0.1 million to Casebia and we and certain of our affiliates entered into an intellectual property contribution agreement with Casebia, or the CRISPR IP Contribution Agreement, as

discussed below, exclusively licensing our CRISPR/Cas technology to Casebia for the purpose of developing and commercializing therapeutic products in certain specified fields, or the Casebia Fields. Bayer Healthcare contributed an initial amount of $45 million at the Closing to Casebia and is committed to contribute up to an additional $255 million in additional funds over time to fund the operations of Casebia, subject to the conditions and procedures discussed below. We and Bayer Healthcare each hold a 50%, non-transferable interest in Casebia. Casebia will sublease a portion of our Cambridge office for its initial operations.

Casebia's initial focus will be within the areas of hematology, ophthalmology and cardiology, in addition to select indications related to other sensory organs, metabolic diseases and autoimmune diseases. Within these areas of focus, we and Bayer Healthcare each have exclusive rights to specified disease indications, the CRISPR Field and Bayer Field, respectively, as discussed below.

Governance

Axel Bouchon, the head of Bayer LifeScience Center, is serving as the initial chief executive officer, or CEO, of Casebia. Casebia is generally governed by a management board, or the Management Board, which is initially comprised of four voting members, two of which are designated by us and two of which are designated by Bayer. In addition, once a CEO unaffiliated with either us or Bayer Healthcare is appointed, he or she will be appointed to the Management Board as a non-voting member. We have initially designated Drs. Novak and Lundberg to serve as our designees to the Management Board. Dr. Novak is also serving as the chairman of the Management Board. Decisions of the Management Board are generally made by majority vote, with each member having one vote. Certain matters require the consent of Bayer Healthcare and us.

Budget And Funding

The JV Agreement sets forth the initial 24-month budget for Casebia, which will be revised by the Management Board on a yearly basis for the following 24 months. Bayer Healthcare, subject to certain conditions, is solely responsible for providing Casebia with the necessary additional funding as determined by the Management Board until its aggregate additional commitment amount of $255 million is fully funded, at which point all additional financing must be approved by the Management Board. Any additional funding beyond the amounts initially committed by Bayer Healthcare in the JV Agreement up to the $300 million aggregate commitment amount, whether for purposes of an acquisition or otherwise, will not affect or dilute our 50% interest in Casebia.

Non-Competition

During the term of the JV Agreement, neither we nor Bayer Healthcare, nor any of our respective affiliates, may develop, commercialize or otherwise exploit any competing product utilizing the CRISPR/Cas technology in any of the Casebia Fields unless, in the case of CRISPR or one of our affiliates, a target is the subject of a pre-existing license or an approved third party agreement, or certain other excluded targets. In addition, in the event either we, Bayer Healthcare or a third party license a product candidate from Casebia pursuant to the Option Agreement discussed below, the non-licensing party or parties to the JV Agreement will be prohibited from developing, commercializing or otherwise exploiting any product utilizing CRISPR/Cas technology to target the same target as that of the licensed product candidate in any of the fields covered by such Option Agreement, so long as the licensing party is clinically developing, commercializing or otherwise exploiting such licensed product candidate.

Furthermore, upon a termination by either party for specified breaches of the other party, the defaulting party will be prohibited from utilizing the CRISPR/Cas technology to develop, commercialize or otherwise exploit product candidates in the field of the terminating party which would be competitive with the terminating party, for a period of two years following such termination.

Termination

The JV Agreement can be terminated by Bayer Healthcare and us upon mutual written consent. Either party may terminate the JV Agreement in the event of specified breaches by the other party or in the event the other party becomes subject to specified bankruptcy, winding up or similar circumstances. Either party may also terminate upon a change of control of the other party and Bayer Healthcare has the right to terminate for good cause, each as defined in the JV Agreement. The JV Agreement may also be terminated by either party if, subsequent to the time that Bayer Healthcare has funded its entire $300 million commitment, the Management Board is unable to approve and obtain sufficient funding, within the time specified in the JV Agreement, to continue Casebia's operations for the next 18 months. Bayer Healthcare may also terminate the JV Agreement during the 30-day period following March 16, 2017 if we have not satisfied certain conditions.

Subject to certain exceptions, in the event of a termination, all Casebia owned patents, know-how and technology will be jointly owned by us and Bayer Healthcare, with the right to sublicense. Upon termination, subject to certain exceptions, Bayer Healthcare will receive an exclusive license to Casebia CRISPR/Cas technology for all non-human therapeutic uses in the Bayer Field and a non-exclusive license for human therapeutic uses in the Bayer Field. Upon such termination, we will receive an exclusive license to Casebia CRISPR/Cas technology in human therapeutic areas, other than in the Bayer Field, and a non-exclusive license for human therapeutic uses in the Bayer Field. Upon any termination, all rights licensed to Casebia pursuant to the CRISPR IP Contribution Agreement will terminate, except for any rights licensed to third parties or to a party who has exercised an option pursuant to the Option Agreement described below.

IP Contribution Agreement With Casebia

As part of our contribution to Casebia, in March, 2016, we and certain of our affiliates entered into the CRISPR IP Contribution Agreement with Casebia. Pursuant to the CRISPR IP Contribution Agreement, we and certain of our affiliated entities granted Casebia an exclusive, worldwide, fully paid-up, royalty-free license, including the right to sublicense, to the use of our CRISPR/Cas technology to research, develop, produce, commercialize and sell products in the Casebia Fields. As partial consideration for the license, Casebia is required to pay us an aggregate amount of $35 million. The CRISPR IP Contribution Agreement also contains license grants from Casebia to us to various forms of intellectual property developed or in-licensed by Casebia. The CRISPR IP Contribution Agreement will terminate simultaneously with the termination of the JV Agreement, subject to survival of certain licenses granted during the term, including licenses granted pursuant to an exercise of an option pursuant to the Option Agreement.

Option Agreement With Bayer

In connection with the Closing, in March, 2016, we, Bayer Healthcare and Casebia entered into an Option Agreement. Pursuant to the Option Agreement, in the event the FDA accepts an IND submitted by Casebia for any product candidate it is developing, both we and Bayer Healthcare have the right to submit an offer to enter into a license with Casebia for the exclusive right to develop, manufacture and commercialize the product candidate in certain Casebia Fields. In addition, Casebia is allowed to receive and consider unsolicited third-party offers, and both we and Bayer Healthcare can require Casebia to seek third-party offers for the applicable product candidate. The Option Agreement sets forth the procedures the Management Board will follow when considering and voting on any offers as well as the considerations on how to value any offer.

Collaboration Agreement With Vertex

On October 26, 2015, we entered into a Strategic Collaboration, Option and License Agreement, or the Collaboration Agreement, with Vertex Pharmaceuticals, Incorporated and Vertex Pharmaceuticals (Europe) Limited, together, Vertex. Pursuant to the Collaboration Agreement, we agreed to provide technology and

options to obtain licenses relating to our CRISPR/Cas technology to Vertex in exchange for a $75 million upfront payment. In connection with the Collaboration Agreement, Vertex also made a $30 million equity investment in us.

Under the Collaboration Agreement, Vertex has the option to exclusively license treatments for up to six collaboration targets that emerge from the four-year research collaboration under certain of our platform and background intellectual property to develop, manufacture, commercialize, sell and use therapeutics directed to each such collaboration target. For any non-hemoglobinopathies targets in-licensed for development, Vertex will pay future development, regulatory and sales milestones of up to $420 million per target, as well as royalty payments in the single digits to low teens on future sales of a commercialized product candidate. The milestone and royalty payments are each subject to reduction under certain specified conditions set forth in the Collaboration Agreement. For these therapies, Vertex is solely responsible for all research, development, manufacturing and global commercialization activities.

However, specifically for hemoglobinopathies targets, if Vertex exercises one or more of its six options on a hemoglobinopathy target, including targets for sickle cell disease, we and Vertex will equally share all development costs and sales expenses. If a hemoglobinopathy target is successfully developed, we would be the lead party responsible for commercialization efforts in the United States and Vertex would be the lead party responsible for commercialization efforts outside the United States. The profits from the sales of any hemoglobinopathies products will be equally shared by Vertex and us.

The initial focus of the collaboration will be to use CRISPR/Cas9 technology to discover and develop gene-based treatments for hemoglobinopathies and cystic fibrosis. Further discovery efforts focused on a specified number of other genetic targets will also be conducted under the Collaboration Agreement. We will be responsible for discovery activities, and the related expenses will be fully funded by Vertex. Under the Collaboration Agreement, we and Vertex have each agreed to certain exclusivity obligations with respect to targets subject to the Collaboration Agreement.

Either party can terminate the Collaboration Agreement upon the other party's material breach, subject to specified notice and core provisions. Vertex also has the right to terminate the Collaboration Agreement for convenience at any time upon 90 days' written notice prior to any product receiving marketing approval and upon 270 days' notice after a product has received marketing approval. In the event we and Vertex make a filing under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, for a collaboration target and such filing is not cleared within a specified time after such filing, the Collaboration Agreement will terminate with respect to that target. We may also terminate the Collaboration Agreement in the event Vertex challenges any of our patent rights.

Absent early termination, the Collaboration Agreement will continue until the expiration of the Vertex's payment obligations under the Collaboration Agreement. Upon termination, the targets that are not licensed by Vertex will be returned to us.

Manufacturing

We currently have no commercial manufacturing or cell processing capabilities. We are working to establish manufacturing processes for both *in vivo* and *ex vivo* CRISPR/Cas9-based therapies. We plan to continue to rely on qualified third-party organizations to produce or process bulk compounds, formulated compounds, viral vectors or engineered cells for IND-supporting activities and early stage clinical trials. We expect that commercial quantities of any compound, vector, or engineered cells that we may seek to develop will be manufactured in facilities and by processes that comply with FDA and other regulations. At the appropriate time in the product development process, we will determine whether to establish manufacturing facilities or continue to rely on third parties to manufacture commercial quantities of any products that we may successfully develop. Outside of the United States and Europe, where appropriate, we may elect in the future to utilize

strategic partners, distributors or contract sales forces to assist in the commercialization of our products. In certain instances, we may consider building our own commercial infrastructure.

As product candidates advance through our pipeline, our commercial plans may change. In particular, some of our research programs target potentially larger indications. Data, the size of the development programs, the size of the target market, the size of a commercial infrastructure and manufacturing needs may all influence our strategies in the United States, Europe and the rest of the world.

Competition

The biotechnology and pharmaceutical industries, including in the gene therapy and gene editing fields, are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on intellectual property and proprietary products. While we believe that our technology, development experience, and scientific knowledge provide us with competitive advantages, we currently face, and will continue to face, competition from many different sources, including major pharmaceutical, specialty pharmaceutical, and biotechnology companies, academic institutions and governmental agencies, and public and private research institutions. For any products that we may ultimately commercialize, not only will we compete with any existing therapies and those therapies currently in development, we will have to compete with new therapies that may become available in the future.

We compete in the segments of the pharmaceutical, biotechnology, and other related markets that utilize technologies encompassing genomic medicines to create therapies, including gene editing and gene therapy. There are additional companies that are working to develop therapies in areas related to our research programs.

Our platform and product focus is on the development of therapies using CRISPR/Cas9 technology. Other companies developing CRISPR/Cas9 technology include Intellia Therapeutics, Inc. and Editas Medicine, Inc.

There are additional companies developing therapies using additional gene-editing technologies, including TALENs, meganucleases, and zinc finger nucleases. The companies developing these additional gene-editing technologies include bluebird bio, Cellectis, Poseida Therapeutics, Precision Biosciences, and Sangamo Biosciences. Additional companies developing gene therapy products include Abeona Therapeutics, Avalanche Biotechnologies, Dimension Therapeutics, REGENXBIO, Spark Therapeutics and uniQure. In addition to competition from other gene-editing therapies or gene therapies, any products that we develop may also face competition from other types of therapies, such as small molecule, antibody, or protein therapies.

In addition, many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology, and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our programs are likely to be their efficacy, safety, convenience, and availability of reimbursement.

If our current programs are approved for the indications for which we are currently planning clinical trials, they may compete with other products currently under development, including gene editing and gene therapy

products. Competition with other related products currently under development may include competition for clinical trial sites, patient recruitment, and product sales.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products, including biological products. Some jurisdictions outside of the United States also regulate the pricing of such products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Licensure and Regulation of Biologics in the United States

In the United States, our candidate products would be regulated as biological products, or biologics, under the Public Health Service Act, or PHSA, and the Federal Food, Drug, and Cosmetic Act, or FDCA, and their implementing regulations. The failure to comply with the applicable U.S. requirements at any time during the product development process, including non-clinical testing, clinical testing, the approval process or post-approval process, may subject an applicant to delays in the conduct of a study, regulatory review and approval, and/or administrative or judicial sanctions. These sanctions may include, but are not limited to, the U.S. Food and Drug Administration's, or FDA's, refusal to allow an applicant to proceed with clinical testing, refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, untitled or warning letters, adverse publicity, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, and civil or criminal investigations and penalties brought by the FDA or the Department of Justice, or DOJ, or other governmental entities.

An applicant seeking approval to market and distribute a new biologic in the United States generally must satisfactorily complete each of the following steps:

- preclinical laboratory tests, animal studies and formulation studies all performed in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an investigational new drug, or IND, application for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated, or by a central IRB if appropriate;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency, and purity of the product candidate for each proposed indication, in accordance with the FDA's Good Clinical Practice, or GCP, regulations;
- preparation and submission to the FDA of a Biologics License Application, or BLA, for a biologic product requesting marketing for one or more proposed indications, including submission of detailed information on the manufacture and composition of the product and proposed labeling;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities, including those of third parties, at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods, and controls are adequate to preserve the product's identity, strength, quality, and purity, and, if applicable, the FDA's current good tissue practice, or CGTP, for the use of human cellular and tissue products;

- satisfactory completion of any FDA audits of the non-clinical study and clinical trial sites to assure compliance with GLPs and GCPs, respectively, and the integrity of clinical data in support of the BLA;
- payment of user fees and securing FDA approval of the BLA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, adverse event reporting, and compliance with any post-approval studies required by the FDA.

Preclinical Studies and Investigational New Drug Application

Before testing any biologic product candidate in humans, including a gene therapy product candidate, the product candidate must undergo preclinical testing. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate the potential for efficacy and toxicity in animals. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an Investigational New Drug, or IND, application. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA imposes a clinical hold based on concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research subjects would be exposed to unreasonable and significant health risks. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trials can begin.

As a result, submission of the IND may result in the FDA not allowing the trials to commence or allowing the trial to commence on the terms originally specified by the sponsor in the IND. If the FDA raises concerns or questions either during this initial 30-day period, or at any time during the conduct of the IND study, including safety concerns or concerns due to non-compliance, it may impose a partial or complete clinical hold. This order issued by the FDA would delay either a proposed clinical study or cause suspension of an ongoing study, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigations may proceed or recommence but only under terms authorized by the FDA. This could cause significant delays or difficulties in completing planned clinical studies in a timely manner.

With gene therapy protocols, if the FDA allows the IND to proceed, but the Recombinant DNA Advisory Committee, or RAC, of the National Institute of Health, or NIH, decides that full public review of the protocol is warranted, the FDA will request at the completion of its IND review that sponsors delay initiation of the protocol until after completion of the RAC review process.

Human Clinical Trials in Support of a BLA

Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease to be treated under the supervision of a qualified principal investigator in accordance with GCP requirements. Clinical trials are conducted under study protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and subsequent protocol amendments must be submitted to the FDA as part of the IND.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from a well-designed and well-conducted clinical trial to the FDA in support of the BLA so long as the clinical trial is conducted in compliance with international guidelines for the ethical conduct of clinical research known as good clinical practice, or GCP, and the FDA is able to validate the data from the study through an onsite inspection if the FDA deems it necessary.

Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, subject informed consent, ethical factors, and the safety of human subjects. An IRB must operate in compliance with FDA regulations. The FDA or the clinical trial sponsor may suspend or terminate a clinical trial at any time for various reasons, including a finding that the clinical trial is not being conducted in accordance with FDA requirements or the subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Clinical testing also must satisfy extensive GCP rules and the requirements for informed consent. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group may recommend continuation of the study as planned, changes in study conduct, or cessation of the study at designated check points based on access to certain data from the study. Finally, research activities involving infectious agents, hazardous chemicals, recombinant DNA, and genetically altered organisms and agents may be subject to review and approval of an Institutional Biosafety Committee in accordance with NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may be required after approval.

- ***Phase 1*** clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion, and pharmacodynamics in healthy humans or, on occasion, in patients, such as cancer patients.
- ***Phase 2*** clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials.
- ***Phase 3*** clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, and gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling.

Progress reports detailing the results, if known, of the clinical trials must be submitted at least annually to the FDA. Written IND safety reports must be submitted to the FDA and the investigators within 15 calendar days after determining that the information qualifies for reporting. IND safety reports are required for serious and unexpected suspected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk to humans exposed to the drug, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Additionally, a sponsor must notify FDA within 7 calendar days after receiving information concerning any unexpected fatal or life-threatening suspected adverse reaction.

In some cases, the FDA may approve a BLA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of biologics approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

Special Regulations and Guidance Governing Gene Therapy Products

It is possible that the procedures and standards applied to gene therapy products and cell therapy products may be applied to any CRISPR/Cas9 product candidates we may develop, but that remains uncertain at this point. The FDA has defined a gene therapy product as one that mediates its effects by transcription and/or translation of transferred genetic material and/or by integrating into the host genome and which are administered as nucleic acids, viruses, or genetically engineered microorganisms. The products may be used to modify cells *in vivo* or transferred to cells *ex vivo* prior to administration to the recipient. Within the FDA, the Center for Biologics Evaluation and Research, or CBER, regulates gene therapy products. Within the CBER, the review of gene therapy and related products is consolidated in the Office of Cellular, Tissue and Gene Therapies, and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. The CBER works closely with the NIH and the RAC, which makes recommendations to the NIH on gene therapy issues and engages in a public discussion of scientific, safety, ethical, and societal issues related to proposed and ongoing gene therapy protocols. The FDA and the NIH have published guidance documents with respect to the development and submission of gene therapy protocols.

Although the FDA has indicated that its guidance documents regarding gene therapies are not legally binding, we believe that our compliance with them is likely necessary to gain approval for any product candidate we may develop. The guidance documents provide additional factors that the FDA will consider at each of the above stages of development and relate to, among other things, the proper preclinical assessment of gene therapies; the chemistry, manufacturing, and control information that should be included in an IND application; the proper design of tests to measure product potency in support of an IND or BLA application; and measures to observe delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high. Further, the FDA usually recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire.

If a gene therapy trial is conducted at, or sponsored by, institutions receiving NIH funding for recombinant DNA research, a protocol and related documentation must submitted to, and the study registered with, the NIH Office of Biotechnology Activities, or OBA, pursuant to the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules prior to the submission of an IND to the FDA. In addition, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. The NIH will convene the Recombinant DNA Advisory Committee, or RAC, a federal advisory committee, to discuss protocols that raise novel or particularly important scientific, safety or ethical considerations at one of its quarterly public meetings. The OBA will notify the FDA of the RAC's decision regarding the necessity for full public review of a gene therapy protocol. RAC proceedings and reports are posted to the OBA web site and may be accessed by the public.

Finally, to facilitate adverse event reporting and dissemination of additional information about gene therapy trials, the FDA and the NIH established the Genetic Modification Clinical Research Information System, or GeMCRIS. Investigators and sponsors of a human gene transfer trials can utilize this web-based system to report serious adverse events and annual reports. GeMCRIS also allows members of the public to access basic reports about human gene transfer trials registered with the NIH and to search for information such as trial location, the names of investigators conducting trials, and the names of gene transfer products being studied.

Compliance with cGMP and CGTP Requirements

Before approving a BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in full compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PHSA emphasizes the importance of manufacturing control for products like biologics whose attributes cannot be precisely defined.

For a gene therapy product, the FDA also will not approve the product if the manufacturer is not in compliance with CGTP. These requirements are found in FDA regulations that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue based products, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the CGTP requirements is to ensure that cell and tissue based products are manufactured in a manner designed to prevent the introduction, transmission, and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through screening and testing.

Manufacturers and others involved in the manufacture and distribution of products must also register their establishments with the FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether foreign or domestic, is deemed misbranded under the FDCA. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated.

Review and Approval of a BLA

The results of product candidate development, preclinical testing, and clinical trials, including negative or ambiguous results as well as positive findings, are submitted to the FDA as part of a BLA requesting a license to market the product. The BLA must contain extensive manufacturing information and detailed information on the composition of the product and proposed labeling as well as payment of a user fee.

The FDA has 60 days after submission of the application to conduct an initial review to determine whether it is sufficient to accept for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or the PDUFA, the FDA has ten months in which to complete its initial review of a standard application and respond to the applicant, and six months for a priority review of the application. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs. The review process may often be significantly extended by FDA requests for additional information or clarification. The review process and the PDUFA goal date may be extended by three months if the FDA requests or if the applicant otherwise provides through the submission of a major amendment additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Under the PHSA, the FDA may approve a BLA if it determines that the product is safe, pure, and potent and the facility where the product will be manufactured meets standards designed to ensure that it continues to be safe, pure, and potent.

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA audits of non-clinical study and clinical trial sites to assure compliance with GLPs and GCPs, respectively, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. If the application is not approved, the FDA will issue a complete response letter, which will contain the conditions that must be met in order to secure final approval of the application, and when possible will outline recommended actions the sponsor might take to obtain approval of the application. Sponsors that receive a complete response letter may submit to the FDA information that represents a complete response to the issues identified by the FDA. Such resubmissions are classified under PDUFA as either Class 1 or Class 2. The classification of a resubmission is based on the information submitted by an applicant in response to an action letter. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has two months to

review a Class 1 resubmission and six months to review a Class 2 resubmission. The FDA will not approve an application until issues identified in the complete response letter have been addressed.

The FDA may also refer the application to an advisory committee for review, evaluation, and recommendation as to whether the application should be approved. In particular, the FDA may refer applications for novel biologic products or biologic products that present difficult questions of safety or efficacy to an advisory committee. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates, and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

If the FDA approves a new product, it may limit the approved indications for use of the product. It may also require that contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may call for post-approval studies, including Phase 4 clinical trials, to further assess the product's safety after approval. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, specific or special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, certain manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, and priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the application is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process, or if the designated drug development program is no longer being pursued.

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product

sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting adverse reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally could support accelerated approval where a study demonstrates a relatively short-term clinical benefit in a chronic disease setting in which assessing durability of the clinical benefit is essential for traditional approval, but the short-term benefit is considered reasonably likely to predict long-term benefit.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Post-Approval Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA has imposed as part of the approval process. The sponsor will be required to report certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official lot release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency, and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, untitled or warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of licensed and approved products that are placed on the market. Pharmaceutical products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Orphan Drug Designation

Orphan drug designation in the United States is designed to encourage sponsors to develop products intended for rare diseases or conditions. In the United States, a rare disease or condition is statutorily defined as a condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and

making available the biologic for the disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation qualifies a company for tax credits and market exclusivity for seven years following the date of the product's marketing approval if granted by the FDA. An application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. A product becomes an orphan when it receives orphan drug designation from the Office of Orphan Products Development, or OOPD, at the FDA based on acceptable confidential requests made under the regulatory provisions. The product must then go through the review and approval process for commercial distribution like any other product.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first drug. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation.

The period of exclusivity begins on the date that the marketing application is approved by the FDA and applies only to the indication for which the product has been designated. The FDA may approve a second application for the same product for a different use or a second application for a clinically superior version of the product for the same use. The FDA cannot, however, approve the same product made by another manufacturer for the same indication during the market exclusivity period unless it has the consent of the sponsor or the sponsor is unable to provide sufficient quantities.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, a BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months.

This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, which was signed into law in March 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. To date, two biosimilar products have been approved by the FDA for use in the United States. No interchangeable biosimilars, however, have been approved. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Additional guidances are expected to be finalized by the FDA in the near term.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Patent Term Restoration and Extension

A patent claiming a new biologic product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of an IND and the submission date of a marketing application, plus the time between the submission date of the marketing application and the ultimate approval date, less any time the applicant failed to act with due diligence. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Regulation And Procedures Governing Approval Of Medicinal Products In The European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary

approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the European Union, or EU, generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the European Medicines Agency, or EMA, or the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by the EMA or these authorities before the product can be marketed and sold in the EU.

Clinical Trial Approval

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Commission Directive 2005/28/EC on GCP, a system for the approval of clinical trials in the EU has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of an EU member state in which the clinical trial is to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member states. Furthermore, the applicant may only start a clinical trial at a specific study site after the ethics committee has issued a favorable opinion. The clinical trial application, or CTA, must be accompanied by an investigational medicinal product dossier with supporting information prescribed by Directive 2001/20/EC and Commission Directive 2005/28/EC and corresponding national laws of the member states and further detailed in applicable guidance documents.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation (EU) No 536/2014 will become applicable no earlier than May 28, 2016. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new legislation, which will be directly applicable in all member states, aims at simplifying and streamlining the approval of clinical trials in the EU. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure via a single entry point and strictly defined deadlines for the assessment of clinical trial applications.

Marketing Authorization

To obtain a marketing authorization for a product under the EU regulatory system, an applicant must submit an MAA, either under a centralized procedure administered by the European Medicines Agency, or EMA, or one of the procedures administered by competent authorities in EU Member States (decentralized procedure, national procedure, or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the EU. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, an applicant must demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Specifically, the grant of marketing authorization in the European Union for products containing viable human tissues or cells such as gene therapy medicinal products is governed by Regulation (EC) No 1394/2007 on advanced therapy medicinal products, read in combination with Directive 2001/83/EC of the European Parliament and of the Council, commonly known as the Community code on medicinal products.

Regulation (EC) No 1394/2007 lays down specific rules concerning the authorization, supervision, and pharmacovigilance of gene therapy medicinal products, somatic cell therapy medicinal products, and tissue engineered products. Manufacturers of advanced therapy medicinal products must demonstrate the quality, safety, and efficacy of their products to EMA which provides an opinion regarding the application for marketing authorization. The European Commission grants or refuses marketing authorization in light of the opinion delivered by EMA.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for conducting an initial assessment of a product. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts such a request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that it is no longer appropriate to conduct an accelerated assessment.

Regulatory Data Protection in the European Union

In the European Union, new chemical entities approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Regulation (EC) No 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for a period of eight years. During the additional two-year period of market exclusivity, a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To that end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least nine months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the drug on the EU market (in the case of the centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid.

Regulatory Requirements after Marketing Authorization

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product. These include compliance with the EU's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. In addition, the manufacturing of

authorized products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's GMP requirements and comparable requirements of other regulatory bodies in the EU, which mandate the methods, facilities, and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. Finally, the marketing and promotion of authorized products, including advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union under Directive 2001/83/EC, as amended.

Orphan Drug Designation and Exclusivity

Regulation (EC) No 141/2000 and Regulation (EC) No 847/2000 provide that a product can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (i) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (ii) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug will be of significant benefit to those affected by that condition.

An orphan drug designation provides a number of benefits, including fee reductions, regulatory assistance, and the ability to apply for a centralized EU marketing authorization. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, neither the European Commission nor the member states can accept an application or grant a marketing authorization for a "similar medicinal product." A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation because, for example, the product is sufficiently profitable not to justify market exclusivity.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may seek regulatory approval by the FDA or other government authorities. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use any product candidates we may develop unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of such product candidates. Even if any product candidates we may develop are approved, sales of such product candidates will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers, and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such product candidates. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A

decision by a third-party payor not to cover any product candidates we may develop could reduce physician utilization of such product candidates once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of pharmaceuticals have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement, and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for any product candidates we may develop will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of any product candidates we may develop to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies (so called health technology assessments, or HTAs) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. E.U. member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic, and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union Member States, and parallel trade (arbitrage between low-priced and high-priced member states), can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of pharmaceutical products that are granted marketing approval. Arrangements with providers, consultants, third-party payors, and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other

healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil U.S. False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious, or fraudulent or knowingly making, using, or causing to be made or used a false record or statement to avoid, decrease, or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the U.S. False Claims Act;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal Health Insurance Portability and Accountability Act, or HIPAA, as amended by the U.S. Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations with respect to safeguarding the privacy, security, and transmission of individually identifiable information that constitutes protected health information, including mandatory contractual terms and restrictions on the use and/or disclosure of such information without proper authorization;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the U.S. Patient Protection and Affordable Care Act, as amended by the U.S. Health Care and Education Reconciliation Act, collectively the Affordable Care Act or ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, and requires certain manufacturers and appliacble group purchasing organizations to report ownership and investment interests held by physicians or their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring pharmaceutical manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the ACA of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable products to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient products to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products. However, the IPAB implementation has been not been clearly defined. The ACA provided that under certain circumstances IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription product spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers, and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal, and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenues from product candidates that we

may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop product candidates.

Additional Regulation

In addition to the foregoing, state, and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act, and the Toxic Substances Control Act, affect our business. These and other laws govern the use, handling, and disposal of various biologic, chemical, and radioactive substances used in, and wastes generated by, operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. Equivalent laws have been adopted in third countries that impose similar obligations.

Employees

As of April 30, 2016 we had 55 full-time employees, 30 of whom held Ph.D. or M.D. degrees, 46 of whom were engaged in research and development, and nine of whom were engaged in business development, finance, information systems, facilities, human resources, legal functions, or administrative support. None of our employees is represented by a labor union, and none of our employees has entered into a collective bargaining agreement with us. We consider our employee relations to be good.

Facilities

Our principal executive offices are located in Basel, Switzerland, where we occupy approximately 365 square feet of office and laboratory space. We do not have a written lease agreement for our occupancy of this space but are working to finalize a formal lease agreement. We also have offices in Cambridge, Massachusetts, where we lease approximately 19,817 square feet of office and laboratory space. Our lease for our Cambridge, Massachusetts office and laboratory space expires February 15, 2022. We also lease approximately 350 square feet of space in London, England. This lease expires July 31, 2016. We believe that our facilities are adequate for our current needs and that suitable additional or substitute space would be available if needed.

Legal Proceedings

From time to time, we may become involved in litigation or other legal proceedings relating to claims arising from the ordinary course of business. There are currently no claims or actions pending against us that, in the opinion of our management, are likely to have a material adverse effect on our business. In January 2016, the U.S. Patent and Trademark Office, or USPTO, declared an interference between one of the pending U.S. patent applications we have in-licensed from Dr. Emmanuelle Charpentier and twelve issued U.S. patents and one U.S. patent application owned jointly by the Broad Institute and Massachusetts Institute of Technology and, in some instances, the President and Fellows of Harvard College, which we refer to individually and collectively as Broad. An interference is a proceeding conducted at the USPTO by the Patent Trial and Appeal Board, or PTAB, to determine which party was first to invent subject matter by at least two parties. There are currently two parties to this interference. Our in-licensed patent application is co-owned among Dr. Emmanuelle Charpentier, the Regents of the University of California and the University of Vienna, whom the USPTO designated collectively as “Senior Party”; Broad was designated as “Junior Party.” Following motions by the parties and other procedural matters, the PTAB could conclude that the contested subject matter is not patentable to the Senior Party, which in this case could preclude Senior Party’s U.S. patent application from issuing a patent; that the contested subject matter is not patentable to the Junior Party, which in this case could result in the cancellation of some or all of the Junior Party’s claims; that the contested subject matter is not patentable to either party; or that the interference should be dismissed. Either party can appeal an adverse decision to the U.S. Court of Appeals for the Federal Circuit. For further information regarding risks regarding the interference and patent rights held by third parties, please see “Risk Factors—Risks Related to Our Intellectual Property.”

MANAGEMENT

Executive Officers and Board of Directors

The following table presents information about our executive officers and directors, including their ages, as of May 9, 2016. The term of each of our directors extends until the next annual general meeting and, accordingly, will expire at the annual general meeting to be held in 2016.

Name	Position	Age
Executive Officers		
Rodger Novak, M.D.	Chief Executive Officer and Director	48
Marc Becker.	Chief Financial Officer	44
Sven Ante (Bill) Lundberg, M.D.	Chief Scientific Officer	52
Samarth Kulkarni, Ph.D.	Chief Business Officer	37
Tyler Dylan-Hyde, Ph.D.	Chief Legal Officer	54
Non-Executive Directors		
N. Anthony Coles, M.D.	Chairman and Director	55
Bradley Bolzon, Ph.D.	Director	56
Ali Behbahani, M.D.	Director	40
Kurt von Emster	Director	48
Simeon J. George, M.D.	Director	39
Thomas Woiwode, Ph.D.	Director	44
Pablo Cagnoni, M.D.	Director	53

(1) Member of the Audit and Finance Committee.
(2) Member of the Compensation, Nomination and Corporate Governance Committee.

The following includes a brief biography for each of our executive officers and directors, with each director biography including information regarding the experiences, qualifications, attributes or skills that caused our board of directors to determine that each member of our board of directors should serve as a director as of the date of this prospectus. There are no family relationships among any of our executive officers or directors.

Executive Officers

Rodger Novak, M.D., Co-Founder, Chief Executive Officer and Director: Dr. Novak co-founded CRISPR Therapeutics AG in November 2013, and has served as a director on our board of directors since inception. Prior to joining our Company, Dr. Novak served as Global Head Anti-infectives Research and Development at Sanofi, a pharmaceutical company. Prior to Sanofi, Dr. Novak co-founded Nabriva Therapeutics AG, a biopharmaceutical company, in January 2006, and served as its Chief Operating Officer from inception to May 2012. From March 2003 to January 2006, Dr. Novak served as the Deputy Head of the Antibiotic Research Institute at Sandoz GmbH. Dr. Novak was appointed as Professor for Microbiology at the Vienna Biocenter in March 2001. Dr. Novak received an M.D. from Philipps University of Marburg, Germany. He continued with post-doctoral work in New York City at The Rockefeller University, St. Jude Children's Research Hospital and the Skirball Institute of Biomolecular Medicine at NYU Langone Medical Center. Dr. Novak has authored numerous publications, including articles in Nature, Nature Medicine and Molecular Cell and is a co-inventor of five patents.

We believe Dr. Novak's experience on our board of directors and as our Chief Executive Officer, as well as his experience in the biopharmaceutical industry, qualifies him to serve on our board of directors.

Marc Becker, Chief Financial Officer: Mr. Becker has served as our Chief Financial Officer since February 2016. Prior to joining our company, Mr. Becker served as Senior Vice President and Chief Financial Officer at rEVO Biologics, Inc., a biopharmaceutical company, from June 2012 to February 2016. Prior to that,

Mr. Becker served various roles at Genzyme Corporation, a biotechnology company, from 2001 to 2011, most recently serving as the Vice President of Finance for the renal and endocrine business unit. Mr. Becker has also held various positions at KPMG LLP and BankBoston (now part of Bank of America). Mr. Becker received an M.B.A. from Babson College and a B.S. in Business Administration from the University of Massachusetts and was licensed as a certified public accountant.

Sven Ante (Bill) Lundberg, M.D., Chief Scientific Officer: Dr. Lundberg has served as our Chief Scientific Officer since February 2015. Prior to joining our company, Dr. Lundberg was Vice President and Head of Translational Medicine at Alexion Pharmaceuticals, Inc., or Alexion, a biopharmaceutical company, from March 2011 to January 2015. From March 2010 to January 2011, Dr. Lundberg was Chief Medical Officer at Taligen Therapeutics, Inc., a biotechnology company that was acquired by Alexion in January 2011, and Vice President of Clinical Development at Antisoma Plc, or Antisoma, from May 2008 to March 2010. Dr. Lundberg also served as Vice President of Clinical Development at Xanthus Pharmaceuticals, Inc. from 2004 until it was acquired by Antisoma in 2008. Previous to that, Dr. Lundberg served as the Medical Director at Wyeth (acquired by Pfizer Inc. in January 2009) and Medical Director at Genzyme Corporation. Dr. Lundberg received an M.D. from Stanford University School of Medicine, an M.B.A. from the Isenberg School of Management at the University of Massachusetts – Amherst, and a B.S. in Biology from the Massachusetts Institute of Technology, or MIT. He completed post-doctoral work at the Whitehead Institute for Biomedical Research at MIT.

Samarth Kulkarni, Ph.D., Chief Business Officer: Dr. Kulkarni has served as our Chief Business Officer since August 2015. Prior to joining our company, Dr. Kulkarni was at McKinsey & Company from 2006 to July 2015, with various titles, his most recent being Partner within the Pharmaceuticals and Biotechnology practice. Dr. Kulkarni received a Ph.D. in Bioengineering and Nanotechnology from the University of Washington and a B. Tech. from the Indian Institute of Technology. Dr. Kulkarni has authored several publications in leading scientific and business journals.

***Tyler Dylan-Hyde, Ph.D., Chief Legal Officer*:** Dr. Dylan-Hyde has served as our Chief Legal Officer since January 2015. Prior to joining our company, Dr. Dylan-Hyde was the Chief Business Officer and General Counsel of Taxus Cardium Partners Group (formerly Cardium Therapeutics, Inc.), from October 2005 to December 2014, and has served as a member of the board of directors since October 2005. Dr. Dylan-Hyde also served as the Chief Business Officer and General Counsel, and a member of the Board of Directors of Tissue Repair Company from August 2006 to November 2014. Prior to that, Dr. Dylan-Hyde was Vice President and General Counsel at Collateral Therapeutics, Inc. (acquired by Schering AG (now Bayer Healthcare Pharmaceuticals) in March 2002), Chief Business Officer and General Counsel at InnerCool Therapies Inc. (acquired by Royal Philips (now ZOLL Medical Corporation) in July 2009), and a Partner at Morrison & Foerster LLP, where he specialized in intellectual property, licensing and corporate transactions. Dr. Dylan-Hyde received a J.D. from the University of California, Berkeley, School of Law, a Ph.D. in Biology from the University of California, San Diego, and a B.Sc. in Cell, Molecular and Developmental Biology from McGill University.

Non-Employee Directors

N. Anthony Coles, M.D., Chairman and Director: Dr. Coles has served on our board of directors since October 2015 as a director and chairman. Dr. Coles also has served as Chief Executive Officer of Yumanity Therapeutics, LLC, a biopharmaceutical company, since October 2014, and as a member of the board of directors of McKesson Corporation, a health care company, since April 2014. From October 2013 to October 2014, Dr. Coles served as Chief Executive Officer of TRATE Enterprises LLC, a privately held company. Dr. Coles also served as President, Chief Executive Officer and member of the board of directors of Onyx Pharmaceuticals, Inc., or Onyx, a biopharmaceutical company, from March 2008 to October 2013, and served as its Chairman since 2012. Prior to joining Onyx, Dr. Coles was President, Chief Executive Officer and a member of the board of directors of NPS Pharmaceuticals, Inc., or NPS, a biopharmaceutical company from November 2005 to March 2008. In addition, Dr. Coles formerly served as a member of the board of directors of Laboratory Corporation of America Holdings, a clinical and specialty testing laboratory company, from December 2010 to March 2012, and

Campus Crest Communities, Inc., a real estate investment trust, from October 2010 to March 2012. Dr. Coles has served on the board of Campus Crest Communities, Inc., a public student housing company. Dr. Coles also serves as a trustee and member of the Executive Committee for the Johns Hopkins University Board of Trustees, as well as a member of the board of trustees for Johns Hopkins Medicine. Dr. Coles received an M.D. from Duke University, an M.P.H. from Harvard University, and a B.S. in Natural Sciences from Johns Hopkins University. We believe Dr. Cole's experience in the biopharmaceutical industry, as well as his experience as a member on the boards of directors of multiple companies in the industry, qualifies him to serve as Chairman of our board of directors.

Bradley Bolzon, Ph.D., Director: Dr. Bolzon has served on our board of directors since November 2013. Dr. Bolzon currently serves as a Managing Director of Versant Venture Management, LLC, where he has been employed since May 2004. Additionally, Dr. Bolzon served as a member of the board of directors of Flexion Therapeutics, Inc., a pharmaceutical company, from its inception in 2007 to June 2014. From February 2000 to May 2004, Dr. Bolzon served as Executive Vice President, Global Head of Business Development, Licensing & Alliances of F. Hoffman-La Roche Ltd., a pharmaceutical company. Dr. Bolzon also formerly served as Head of Cardiovascular Research at Eli Lilly and Company. Dr. Bolzon received a Ph.D. in Pharmacology and an M.S. in Pharmacology from the University of Toronto. He continued with post-doctoral work at the University of Ottawa Heart Institute. We believe Dr. Bolzon's experience in the biopharmaceutical industry qualifies him to serve on our board of directors.

Ali Behbahani, M.D., M.B.A., Director: Dr. Behbahani has served on our board of directors since April 2015. Dr. Behbahani joined New Enterprise Associates, Inc., or NEA, in 2007 and is a Partner on the healthcare team. Dr. Behbahani has also served as a member of the board of directors of Nevro Corp., a medical device company, since August 2014 and Adaptimmune Therapeutics, a biopharmaceutical company, since September 2014. Prior to joining NEA, Dr. Behbahani served as a consultant in business development at The Medicines Company, a pharmaceutical company. In addition, Dr. Behbahani formerly served as a Venture Associate at Morgan Stanley and as a Healthcare Investment Banking Analyst at Lehman Brothers. Dr. Behbahani received an M.D. from the University of Pennsylvania School of Medicine, an M.B.A. from the Wharton School of the University of Pennsylvania and a B.S. in Biomedical Engineering, Electrical Engineering and Chemistry from Duke University. We believe Dr. Behbahani's experience in the biopharmaceutical industry, as well as his experience as a member on the boards of directors of multiple companies in the industry, qualifies him to serve on our board of directors.

Simeon J. George, M.D., Director: Dr. George has served on our board of directors since April 2015. Dr. George currently serves as a Partner at S.R. One, Limited, where he has been employed since 2007. In addition, Dr. George previously served as a director on the boards of the following biotechnology companies: Semprus BioSciencies Corp. (acquired by Teleflex Incorporated in June 2012) from December 2010 to June 2012, HTG Molecular Diagnostics, Inc. from June 2011 to October 2015, and Genocea Biosciences, Inc. from July 2010 to December 2014. Dr. George also served as a consultant at Bain & Company from October 2006 to August 2007. Dr. George received an M.D. from the University of Pennsylvania School of Medicine, an M.B.A. from the Wharton School of the University of Pennsylvania, and a B.A. in Neuroscience from Johns Hopkins University. We believe Dr. George's experience in the biopharmaceutical industry, as well as his experience as a member on the boards of directors of multiple companies in the industry, qualifies him to serve on our board of directors.

Kurt von Emster, Director: Mr. von Emster has served on our board of directors since April 2015. Mr. von Emster currently serves as Managing Partner at Abingworth LLP, where he has been employed as a Partner since January 2015. Mr. von Emster also has served as a member of the board of directors of CymaBay Therapeutics, Inc., a biotechnology company, since April 2009. Mr. von Emster previously served on the board of directors of the following companies: Cytos Biotechnology AG from November 2012 to January 2016 (merged and renamed Kuros Biosciences in January 2016), Aurinia Pharmaceuticals Inc. from February 2014 to March 2015, Facet Biotech Corporation (acquired by Abbott Laboratories in April 2010) from February 2009 to April 2010, and Somaxon Pharmaceuticals (acquired by Pernix Therapeutics in March 2013) from September 2005 to January 2013. In

addition, Mr. von Emster co-founded venBio LLC, a health-care focused investment firm, in 2009, and served as Partner until 2014. Prior to that, Mr. von Emster was General Partner at MPM Capital, Inc., a biotechnology private equity firm, from 2001 to 2009. Mr. von Emster was also a Biotechnology and Healthcare Analyst and Portfolio Manager at Franklin Templeton Group from 1989 to 2000. Mr. von Emster received a B.S. in Business and Economics from the University of California, Santa Barbara. We believe Mr. von Emster's experience in the biotechnology industry, as well as his experience as a member on the boards of directors of multiple companies in the industry, qualifies him to serve on our board of directors.

Thomas F. Woiwode, Ph.D., Director: Dr. Woiwode has served on our board of directors since April 2014. Dr. Woiwode joined Versant Venture Management, LLC, or Versant, in 2002 and has served as a Venture Partner since 2011 and as a Managing Director since July 2014. Dr. Woiwode also has served on the board of directors of Audentes Therapeutics, Inc., a biotechnology company, since July 2013. Dr. Woiwode previously served as the Chief Operating Officer of Okairos, a biopharmaceutical company acquired by GlaxoSmithKline plc in May 2013, from July 2011 to May 2013. In addition, Dr. Woiwode co-founded Euroventures, a wholly owned biotechnology incubator within Versant, and in this role, served as the founding Chief Business Officer of three biotech companies created within Versant. Dr. Woiwode received a Ph.D. in Organic Chemistry at Stanford University and a B.A. in English and a B.S. in Chemistry from the University of California, Berkeley. We believe Dr. Woiwode's experience in the biotechnology industry, as well as his experience as a member on the boards of directors of multiple companies in the industry, qualifies him to serve on our board of directors.

Pablo Cagnoni, M.D., Director: Dr. Cagnoni has served on our board of directors since December 2015. Dr. Cagnoni has also served as Managing Director of MPM Capital, Inc, since May 2015. In addition, Dr. Cagnoni has served as President and Chief Executive Officer of Tizona Pharmaceuticals, Inc., a biotechnology company, since May 2015. Dr. Cagnoni previously served as President of Onyx Pharmaceuticals, Inc. from October 2013 to April 2015, and as Executive Vice President, Global Research and Development and Technical Operations from April 2013 to October 2013. Dr. Cagnoni also served in management roles at the following biotechnology companies: Senior Vice President and Global Head of Clinical Development at Novartis AG from October 2009 to April 2013, Senior Vice President and Chief Medical Officer at Allos Therapeutics, Inc. from March 2007 to September 2009, and Chief Medical Officer and Vice President of Clinical Research and Medical Affairs at OSI Pharmaceuticals, Inc. from July 2004 to March 2007. Dr. Cagnoni was also Assistant Professor of Medicine and Assistant Director Pharmacology Laboratory at the University of Colorado Bone Marrow Transplant Program. Dr. Cagnoni received an M.D. from the University of Buenos Aires School of Medicine. He continued with post-doctoral work in Hematology and Oncology at the Mount Sinai Medical Center and in Stem Cell Transplantation at the University of Colorado Health Sciences Center. We believe Dr. Cagnoni's experience in the biotechnology industry qualifies him to serve on our board of directors.

Scientific Advisory Board

Emmanuelle Marie Charpentier, Ph.D.: Dr. Charpentier is one of our co-founders. Dr. Charpentier is a Scientific Member of the Max Planck Society in Germany, Director at the Max Planck Institute for Infection Biology and an Alexander von Humboldt Professor at the Helmholtz Centre for Infection Research, Braunschweig. Dr. Charpentier also oversees a research group at the Laboratory for Molecular Infection Medicine Sweden at Umeå University. She has held research associate positions at The Rockefeller University, New York University Langone Medical Center, the Skirball Institute of Biomolecular Medicine and the St. Jude Children's Research Hospital. Dr. Charpentier's research unveiled the key mechanisms of the CRISPR/Cas9 technology, laying the foundation for CRISPR/Cas9 as a gene editing tool. She has received over 25 awards for her work on CRISPR/Cas9, including the Breakthrough Prize in Life Sciences and the Massry Prize. In 2015, Dr. Charpentier was recognized by TIME Magazine as one of the 100 most influential people.

Daniel Anderson, Ph.D.: Dr. Anderson is an Associate Professor in Chemical Engineering, the Institute for Medical Engineering and Science and the Harvard-MIT Division of Health Science and Technology at the Massachusetts Institute of Technology, or MIT. He is also an intramural member of the Koch Institute for Integrative Cancer Research at MIT and an associate of the Ragon Institute. Dr. Anderson is widely recognized

as a leader in the development of biomaterials, and his work has led to applications in medical devices, cosmetics, cell therapy and drug therapy. The advanced drug delivery systems developed in his laboratory have provided new methods for gene therapy and gene editing, including the first description of using the CRISPR/Cas9 system to repair a disease gene in an adult animal.

Chad Cowan, Ph.D.: Dr. Cowan is an Associate Professor in the Department of Stem Cell and Regenerative Biology at Harvard University, or Harvard, and an Associate Professor in the Center for Regenerative Medicine, the Cardiovascular Research Center and the Center for Human Genetics Research at Massachusetts General Hospital. He also has appointments in the Center for Regenerative Medicine, the Cardiovascular Research Center and the Center for Human Genetics Research. Dr. Cowan is an associate member of the Broad Institute and a principal faculty member of the Harvard Stem Cell Institute where he directs the Diabetes Disease Program and the iPS Cell Core Facility. Dr. Cowan was named a Stowers Medical Investigator in 2006. Dr. Cowan and his colleagues at Harvard were first to demonstrate the advantages of CRISPR/Cas9 over the older nuclease editing technologies such as TALENs and the effective editing of hematopoietic stem cells and T-cells.

Stephen Elledge, Ph.D.: Dr. Elledge is the Gregor Mendel Professor of Genetics and Medicine at Harvard Medical School and Brigham and Women's Hospital. Dr. Elledge was named an Investigator with the Howard Hughes Medical Institute in 1993. Dr. Elledge is a leading authority on the mechanisms of DNA repair that are essential to CRISPR/Cas9 gene editing approaches and has published over 250 articles, including contributions to the study of proteins and biochemical pathways that regulate the cell division cycle, how cells sense and respond to DNA damage, how cells selectively destroy proteins in response to signals and how these pathways are usurped in human cancer. Dr. Elledge has received numerous awards including the 2015 Albert Lasker Basic Medical Research Award.

Craig Mello, Ph.D.: Dr. Mello is a Professor of the RNA Therapeutics Institute at the University of Massachusetts Medical School and the Blais University Chair in Molecular Medicine. Dr. Mello was named an Investigator at the Howard Hughes Medical Institute in 2000. Dr. Mello is a discoverer of RNA interference (RNAi) and its gene silencing capabilities and with Dr. Andrew Fire received the 2006 Nobel Prize in Physiology or Medicine for such invention. Dr. Mello is a member of the National Academy of Sciences, the American Academy of Arts and Sciences and the American Philosophical Society.

Matthew Porteus, M.D., Ph.D.: Dr. Porteus is an Associate Professor of Pediatrics in the Department of Pediatrics, Divisions of Hematology/Oncology and Human Gene Therapy at Stanford School of Medicine and previous to that, he was an Assistant Professor of Pediatrics and Biochemistry at the University of Texas Southwestern Medical School. Dr. Porteus is an Attending Physician for the Pediatric Bone Marrow Transplant Service at Lucille Packard Children's Hospital. Dr. Porteus trained with Dr. David Baltimore at the Massachusetts Institute of Technology and the California Institute of Technology. During this time, he was the first to show that engineered nucleases could be used to precisely modify human cells by homologous recombination. Dr. Porteus' research focuses on developing homologous recombination-based therapies for genetic and other diseases and he was the first person to use DNA endonuclease technology for gene editing.

Board Composition and Election of Directors After This Offering

Our board of directors is composed of seven members. Each director is elected for a one-year term. The current members of our board of directors were appointed at shareholders' meetings held on October 9, 2015 and December 8, 2015 to serve until the next ordinary shareholders' meeting.

Following the closing of this offering, our compensation, nomination and corporate governance committee and board of directors may consider a broad range of factors relating to the qualifications and background of nominees, which may include diversity and is not limited to race, gender or national origin. We have no formal policy regarding board diversity. Our compensation, nomination and corporate governance committee's and

board of directors' priority in selecting board members is identification of persons who will further the interests of our company through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, and professional and personal experiences and expertise relevant to our growth strategy.

Director Independence

Under the listing requirements and rules of the NASDAQ Global Market, independent directors must comprise a majority of our board of directors as a listed company within one year of the closing of this offering.

Our board of directors has undertaken a review of its composition, the composition of its committees and the independence of each director. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our board of directors has determined that , and do not have any relationships that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the applicable rules and regulations of the Securities and Exchange Commission, or the SEC, and the listing requirements and rules of the NASDAQ Global Market. In making this determination, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director.

Committees of the Board of Directors

Our board of directors has two standing committees: (1) an audit and finance committee and (2) a compensation, nomination and corporate governance committee.

Audit and Finance Committee

Our audit and finance committee consists of , and . Our board of directors has determined that , , and are independent under the NASDAQ listing standards and Rule 10A-3(b)(1) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. The chair of our audit and finance committee is . Our board of directors has determined that is an "audit committee financial expert" within the meaning of SEC regulations. Our board of directors has also determined that each member of our audit and finance committee can read and understand fundamental financial statements in accordance with applicable requirements. In arriving at these determinations, the board of directors has examined each audit and finance committee member's scope of experience and the nature of their employment in the corporate finance sector.

The audit and finance committee will be governed by a charter that complies with NASDAQ rules. Upon the completion of this offering, the audit and finance committee has the responsibility to, among other things:

- review and assess the qualifications, independence, performance and effectiveness of the independent auditor;
- review the scope of the prospective audit by the independent auditor, the estimated fees, and any other matters pertaining to the audit;
- approve any audit and non-audit services proposed to be provided by the independent auditor to ensure independent auditor independence;
- review and assess the independent auditor's report, management letters and take notice of all comments of the independent auditor on accounting procedures and systems of control, and review the independent auditor's reports with management;

- be responsible for the resolution of disagreements between the management and the independent auditor;
- review and evaluate the lead audit partner of the independent audit team and confirm and evaluate their rotation;
- review, discuss with the chief financial officer and the independent auditor and approve (i) the annual and quarterly financial statements, (ii) reports intended for publication and (iii) any other financial statements intended for publication to consider significant financial reporting issues and judgments made in connection with the preparation of our financial statements, including any significant changes in our selection or application of accounting principles;
- review with the management, personnel responsible for the design and implementation of the internal audit function and the independent auditor in separate meetings any analysis or other written communication prepared by the management and/or the independent auditor setting forth significant financial reporting issues and judgments made in connection with the preparation of the financial statements, including critical accounting policies, the effect of regulatory and accounting initiatives, as well as off-balance sheet transactions and structures on our financial statements;
- review and approve our quarterly financial statements for the first three quarters of each calendar year and the corresponding financial results releases;
- review in cooperation with the independent auditor and the management whether the accounting principles applied are appropriate in view of our size and complexity;
- periodically review our policies and procedures for risk management and assess the effectiveness thereof including discussing with management our major financial risk exposures and the steps that have been taken to monitor and control such exposures;
- discuss with management and external advisors any legal matters that may have a material impact on our financial statements and any material reports or inquiries from regulatory or governmental agencies which could materially impact our contingent liabilities and risks;
- review our disclosure controls and procedures and internal control over financial reporting which shall include significant deficiencies and material weaknesses in the design or operation of internal controls over financial reporting;
- recommending, based upon its review and discussions with management and the independent registered public accounting firm, whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- preparing the audit and finance committee report required by the rules of the SEC to be included in our annual proxy statement;
- establish procedures for the receipt, retention and treatment of complaints received regarding accounting, internal accounting controls or auditing matters, and the confidential, anonymous submission by employees of concerns regarding questionable accounting or auditing matters; and
- recommend to the board whether to approve and ratify any related person transaction in accordance with our related person transaction policy.

The audit and finance committee will meet as often as it determines is appropriate to carry out its responsibilities, but in any event will meet at least four times per year.

Compensation, Nomination and Corporate Governance Committee

Our compensation, nomination and corporate governance committee consists of , and . Our board of directors has determined that , and are independent under the NASDAQ listing standards, are “non-employee directors” as defined in Rule 16b-3 promulgated under the Exchange Act and are “outside directors” as that term is defined in Section 162(m) of the Internal Revenue Code

of 1986, as amended, or Section 162(m). The chair of our compensation, nomination and corporate governance committee is . The committee will assist our board of directors in overseeing our cash compensation and equity award recommendations for our executive officers along with the rationale for such recommendations, as well as summary information regarding the aggregate compensation provided to our executive officers. We will be subject to the Swiss Ordinance against excessive compensation in listed stock corporations, known as the "Say on Pay" Rule. This means that the members of the compensation, nomination and corporate governance committee must be elected by the shareholders' meeting and that the compensation of our board of directors and executive officers must be presented by the board of directors to our shareholders and our shareholders must vote on the proposed compensation. The primary purpose of our compensation, nomination and corporate governance committee is to discharge the responsibilities of our board of directors to oversee our compensation policies, plans and programs and to review and determine the compensation to be paid to our executive officers, directors and other senior management, as appropriate.

In addition, this committee will also be responsible for director and board committee nominations as well as reviewing and amending, if required, our corporate governance framework and guidelines.

Upon the completion of this offering, the compensation, nomination and corporate governance committee has the responsibility to, among other things:

- review and approve, or recommend that our board of directors approve, the compensation of our executive officers;
- review and recommend to our board of directors the compensation of our directors;
- review and approve, or recommend that our board of directors approve, the terms of compensatory arrangements with our executive officers;
- administer our share and equity incentive plans;
- select independent compensation consultants and assess whether there are any conflicts of interest with any of the committees' compensation advisers;
- review and approve, or recommend that our board of directors approve, incentive compensation and equity plans, and any other compensatory arrangements for our executive officers and other senior management, as appropriate;
- review and establish general policies relating to compensation and benefits of our employees and reviewing our overall compensation philosophy;
- identify, evaluate and select, or recommend that our board of directors approve, nominees for election to our board of directors;
- evaluate the performance of our board of directors and of individual directors;
- consider and make recommendations to our board of directors regarding the composition of the committees of the board of directors;
- review developments in corporate governance practices;
- evaluate the adequacy of our corporate governance practices and reporting;
- review management succession plans;
- develop and make recommendations to our board of directors regarding corporate governance guidelines and matters; and
- oversee an annual evaluation of the board of directors' performance.

Compensation, Nomination and Corporate Governance Committee Interlocks and Insider Participation

None of the members of the compensation, nomination and corporate governance committee is currently, or has been at any time, one of our officers or employees. None of our executive officers currently serves, or has served during the last year, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving as a member of our board of directors or compensation, nomination and corporate governance committee.

Code of Business Conduct and Ethics

In connection with this offering, we will adopt a Code of Business Conduct and Ethics, or the Code of Conduct, that is applicable to all of our employees, executive officers and directors. Following the completion of this offering, the Code of Conduct will be available on our website www.crisprtx.com. The audit and finance committee of our board of directors will be responsible for overseeing the Code of Conduct and will be required to approve any waivers of the Code of Conduct for employees, executive officers and directors. We expect that any amendments to the Code of Conduct, or any waivers of its requirements, will be disclosed on our website.

EXECUTIVE AND DIRECTOR COMPENSATION

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to each of our named executive officers during the fiscal years ended December 31, 2015.

Name	Year	Salary ($)	Bonus ($)	Share Awards ($)(1)	Option Awards ($)(1)	Non-Equity Incentive Plan Compensation ($)(2)	All Other Compensation ($)(3)	Total ($)
Rodger Novak, M.D.(4) *Chief Executive Officer*	2015	$ 356,242	—	$ 326,360	$ 820,587	$ 118,424	$ 66,968	$ 1,688,581
Sven Ante Lundberg, M.D. *Chief Scientific Officer*	2015	$ 302,605	$ 38,356(5)	$ 1,760,400	—	$ 90,928	$ 383,513	$ 2,575,802
Samarth Kulkarni, Ph.D. *Chief Business Officer*	2015	$ 145,833	—	$ 277,074	$ 984,708	$ 43,750	$ 152	$ 1,451,517

(1) Amounts represent the aggregate grant date fair value of stock and option awards granted to our named executive officers in 2015 computed in accordance with FASB ASC Topic 718. Pursuant to FASB ASC Topic 718, the amounts shown exclude the impact of estimated forfeitures related to service-based vesting conditions. For awards with award conditions, the amounts reported are based upon probable outcome, which for this purpose was determined to be the maximum level of achievement. For additional information on the valuation assumptions underlying the value of these awards, see the notes to our consolidated financial statements and discussions included elsewhere in this prospectus. The amounts above reflect our aggregate accounting expense for these awards and do not necessarily correspond to the actual value that will be recognized by the named executive officers.

(2) Amounts represent incentive compensation paid to our named executive officers for 2015 performance based upon achievement of certain corporate goals, business development objectives and research and development milestones.

(3) Amounts reported include (i) for Dr. Novak, $59,637 in pension contributions as required under Swiss law and (ii) for Dr. Lundberg, $383,513 as a bonus to purchase restricted shares and offset the tax liability associated with such purchase.

(4) The compensation paid to Dr. Novak in CHF has been converted from CHF to USD at an exchange rate of 0.9628 CHF:1 USD based on the average daily noon buying rate of exchange of the Federal Reserve Bank of New York for 2015.

(5) Amount represents a signing bonus paid to Dr. Lundberg in connection with his commencement of employment with us.

Employment Agreements with Our Named Executive Officers and Key Employees

We have entered into employment agreements with each of our named executive officers. We designed these agreements to be part of a competitive compensation package and to keep our executive officers focused on our business goals and objectives. These agreements provide for base salaries and incentive compensation benefits, and each component reflects the scope of each named executive officer's anticipated responsibilities and the individual experience they bring to the company.

Dr. Rodger Novak. We entered into an employment agreement with Dr. Novak in November 2013, for the position of Chief Executive Officer. Pursuant to Dr. Novak's employment agreement, he was entitled to an initial annual base salary of CHF 350,000, which was increased to CHF 410,000 effective September 1, 2015. Dr. Novak is eligible for annual performance bonuses. Dr. Novak's annual target bonus was initially set at 30% of his annual base salary. Under Dr. Novak's employment agreement, Dr. Novak is entitled to three months' notice if his employment is terminated without just cause in accordance with Swiss law.

Dr. Sven Ante Lundberg. We entered into an employment agreement with Dr. Lundberg in February 2015, for the position of Chief Scientific Officer. Pursuant to Dr. Lundberg's employment agreement, he is

entitled to an initial annual base salary of $350,000 and received a one-time starting bonus of $38,356. Dr. Lundberg is eligible for annual performance bonuses based upon criteria established by our Chief Executive Officer and Dr. Lundberg. Dr. Lundberg's annual target bonus was initially set at 30% of his annual base salary. Dr. Lundberg also purchased 135,000 of our restricted common shares. Of this total amount, 120,000 restricted shares are subject to a right of repurchase by us that will lapse ratably in monthly installments beginning on March 1, 2015 and ending on the fourth anniversary of the commencement date of Dr. Lundberg's employment, subject to Dr. Lundberg's continued employment with us. The remaining 15,000 restricted shares are also subject to a right of repurchase by us beginning on or within 60 days following the earlier to occur of (i) the termination of Dr. Lundberg's employment with us and (ii) August 18, 2016. The repurchase rights applicable to the 15,000 restricted shares will lapse upon the achievement of specified performance metrics set forth in the employment agreement. Additionally, Dr. Lundberg was granted a one-time special purpose bonus in cash equal to the aggregate purchase price of his restricted shares. Dr. Lundberg is eligible to participate in our employee benefit plans on the same terms as other senior executives.

Dr. Lundberg's employment agreement further provides that in the event his employment is terminated without "cause," as defined in his employment agreement, or he terminates his employment for "good reason," as defined in his employment agreement, he is entitled to receive (i) an amount equal to 50% of his base salary and 50% of his target bonus and (ii) copayment of Dr. Lundberg's COBRA premiums until the earlier of (1) 18 months following the termination, (2) the date Dr. Lundberg obtains full time employment and (3) the expiration of Dr. Lundberg's rights under COBRA. In addition, all vesting or similar restrictions on any equity awards held by Dr. Lundberg that would have vested or the restrictions would otherwise have lapsed during the six month period following the date of Dr. Lundberg's termination shall vest and become exercisable or nonforfeitable.

In the event that Dr. Lundberg is (i) terminated within 18 months following a change in control without "cause" or (ii) he terminates his employment for any reason within 18 months following a change in control and after remaining employed by us (or our successor) for six months following a change of control, then Dr. Lundberg shall be entitled to receive (i) an amount equal to one times his base salary and target bonus and (ii) copayment of Dr. Lundberg's COBRA premiums until the earlier of (1) 18 months following the termination, (2) the date Dr. Lundberg obtains full time employment and (3) the expiration of Dr. Lundberg's rights under COBRA. In addition, all of the restricted shares and options granted to Dr. Lundberg will accelerate and vest in full. To the extent Section 280G of the Internal Revenue Code of 1986, as amended, is applicable to such change in control, Dr. Lundberg will be entitled to receive the better treatment of: (i) payment of the full amounts set forth above to which he is entitled or (ii) payment of such lesser amount that does not trigger excise taxes under Section 280G.

Dr. Samarth Kulkarni. We entered into an employment agreement with Dr. Kulkarni in July 2015, for the position of Chief Business Officer. Pursuant to Dr. Kulkarni's employment agreement, he is entitled to an initial annual base salary of $350,000. Dr. Kulkarni is eligible for annual performance bonuses based upon criteria established by our board. Dr. Kulkarni's annual target bonus was initially set at 30% of his annual base salary. Dr. Kulkarni also was issued 40,214 restricted shares, with 25% of such restricted shares vesting at the one year anniversary of Dr. Kulkarni's commencement of employment, and 1/36 of such restricted shares vesting each month thereafter. In addition to the restricted shares, Dr. Kulkarni was granted an option to purchase 96,514 common shares. Of these, 80,429 shares under the option are subject to time-based vesting, with 25% of the shares vesting at the one year anniversary of Dr. Kulkarni's commencement of employment, and 1/36 of the shares vesting each month thereafter. The remaining 16,085 shares under the option are subject to performance based vesting that vest at the one year commencement of Dr. Kulkarni's employment, subject to the achievement of specified performance metrics. The offer letter also provided Dr. Kulkarni up to $70,000 of expense reimbursement in connection with his relocation to the greater Boston, Massachusetts area and five months of temporary housing. Dr. Kulkarni is eligible to participate in our employee benefit plans on the same terms as other regular, full-time employees.

Dr. Kulkarni's employment agreement further provides that in the event his employment is terminated without "cause," as defined in his employment agreement, or he terminates his employment for "good reason," as defined in his employment agreement, he is entitled to receive his then monthly base salary and target bonus until the earlier of (i) six months following the termination or (2) the date Dr. Kulkarni commences full time employment. In addition, any reacquisition or repurchase rights we hold with respect to the options granted to Dr. Kulkarni pursuant to the employment agreement shall lapse for the portion of such equity awards which would otherwise have vested during the six month period following the date of Dr. Kulkarni's termination.

In the event that Dr. Kulkarni is (i) terminated (A) within 18 months following or (B) three months prior to a change in control without "cause" or (ii) he terminates his employment after six months following a change of control for "good reason," then all of the options granted to Dr. Kulkarni pursuant to his employment agreement will vest in full.

Marc Becker. We entered into an employment agreement with Mr. Becker in January 2016, for the position of Chief Financial Officer. Pursuant to Mr. Becker's employment agreement, he is entitled to an initial annual base salary of $330,000 and received a one-time starting bonus of $101,500. Mr. Becker is eligible for annual performance bonuses based upon criteria established by our board. Mr. Becker's annual target bonus was initially set at 30% of his annual base salary. Mr. Becker was also granted an option to purchase 84,578 common shares. The options are time-based options, with 25% of the option vesting at the one year anniversary of Mr. Becker's commencement of employment, and 1/36 of the remaining option vesting each month thereafter. Mr. Becker is eligible to participate in our employee benefit plans on the same terms as other senior executives.

Mr. Becker's employment agreement further provides that in the event his employment is terminated without "cause," as defined in his employment agreement, or he terminates his employment for "good reason," as defined in his employment agreement, he is entitled to receive half of his then current base salary and half of his target bonus, paid equally over a six-month period following the termination. In addition, any vesting with respect to the options granted to Mr. Becker pursuant to his employment agreement shall lapse for the portion of such equity awards as to which such reacquisition or repurchase rights would have otherwise vested during the six month period following the date of Mr. Becker's termination.

In the event that Mr. Becker is (i) terminated within twelve months following a change in control without "cause" or (ii) he terminates his employment after twelve months following a change of control for "good reason," then all of the options granted to Mr. Becker pursuant to his employment agreement will vest in full. In addition, Mr. Becker would be entitled to receive a one-time payment equal to his then current base salary plus his target bonus.

Employee Confidentiality, Non-Competition, Non-solicitation And Assignment Agreements

Each of our named executive officers has entered into agreements with respect to confidential information and assignment of inventions. Among other things, this agreement obligates each named executive officer to refrain from disclosing any of our proprietary information received during the course of employment and to assign to us any inventions conceived or developed during the course of employment. In addition, this agreement also subjects each of our named executive officers to certain non-competition and/or non-solicitation obligations as set forth in their respective agreements.

Indemnification Agreements

In connection with this offering, we intend to enter into indemnification agreements with each of our directors and executive officers. See the section of this prospectus titled "Description of Share Capital and Articles of Association—Indemnification of Executive Management and Directors."

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

2015 Outstanding Equity Awards at Fiscal Year-End

The following table sets forth information concerning outstanding equity awards for each of our named executive officers at December 31, 2015:

	Option Awards(1)					Stock Awards(1)			
Name	Vesting Commencement Date	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested (#)(2)	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (#)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units or Other Rights That Have Not Vested ($)(2)
Rodger Novak, M.D.	9/10/2015	33,511(3)	46,917(3)	6.15	9/10/2025	—	—	—	—
Sven Ante Lundberg, M.D.	2/18/2015	—	—	—	—	110,000(4)(5)	$2,110,900	15,000(5)(6)	$ 287,850
Samarth Kulkarni, Ph.D.	8/1/2015	0	16,085(7)(8)	6.15	9/10/2025	—	—	—	—
	8/1/2015	0	80,429(4)(8)	6.15	9/10/2025	—	—	—	—
	8/1/2015	—	—	—	—	40,214(4)(8)	$ 771,707	—	—

(1) Except in the case of Dr. Lundberg's restricted shares, each award was granted pursuant to our 2015 Stock Option and Grant Plan. Unless otherwise specified below, each award vests with respect to 25% of the shares on the first anniversary of the vesting commencement date and the remaining 75% vests in equal monthly installments over the next three years thereafter, subject to continuous service through each such date.

(2) The market value is calculated by multiplying the number of unvested shares by $19.19, which was the fair market value of the Company's common shares as of December 31, 2015.

(3) This option was vested with respect to 28,484 of the shares subject to the option as of the vesting commencement date, with the remaining 51,944 shares subject to the option vesting ratably over 31 months thereafter, subject to continuous service through each such date.

(4) If the executive's employment is terminated without cause or he resigns for good reason, subject to delivery of a release, this award shall accelerate and vest as if such executive had remained employed for an additional six months.

(5) In the case of a change in control, this award shall accelerate and vest in full if (i) the executive's employment is terminated without cause within 18 months following such change in control or (ii) the executive resigns after six months following such change in control.

(6) This restricted share award is subject to vesting upon achievement of certain performance criteria on or prior to August 18, 2016. If Dr. Lundberg's employment is terminated without cause or he resigns for good reason prior to such date, then a number of shares equal to the number of then-unvested shares (which have not otherwise been forfeited) as of such date, multiplied by a fraction, the numerator of which is the lesser of 180 days or the number of days remaining until August 18, 2016, and the denominator of which is the number of days remaining until August 18, 2016.

(7) 100% of the shares subject to this option vest and become exercisable as of the vesting commencement date, provided that certain performance criteria have been met as of July 31, 2016 and Dr. Kulkarni continues to have a service relationship with us as of such date. As of December 31, 2015, the applicable performance

criteria had been met. If Dr. Kulkarni's employment is terminated without cause or he resigns for good reason on or after February 1, 2016 and prior to August 1, 2016, subject to delivery of a release, then 100% of this option shall vest and become exercisable as of the effectiveness of such release.

(8) In the case of a change in control, this award shall accelerate and vest in full if (i) the executive's employment is terminated without cause within 18 months following such change in control, (ii) the executive's employment is terminated without cause after we have taken substantial steps to negotiate a change in control agreement and such change in control actually occurs within three months thereafter or (iii) the executive resigns after six months following such change in control.

Director Compensation

The following table sets forth a summary of the compensation we paid to our nonemployee directors during 2015. Other than as set forth in the table and described more fully below, we did not pay any compensation, reimburse any expense of, make any equity awards or non-equity awards to, or pay any other compensation to any of the other nonemployee members of our board of directors in 2015. We reimburse nonemployee directors for reasonable travel expenses. Dr. Novak, our Chief Executive Officer, receives no compensation for his service as a director, and, consequently, is not included in this table. The compensation received by Dr. Novak as an employee during 2015 is presented in the "Summary Compensation Table" above.

Name	Fees Earned or Paid In Cash ($) (1)	Option Awards ($) (2)	All Other Compensation ($) (3)	Total ($)
N. Anthony Coles, M.D.(4)	$ 11,507	$820,587	$ 50,000	$882,094
Bradley Bolzon, Ph.D.	—	—	—	—
Ali Behbahani, M.D.	—	—	—	—
Simeon J. George, M.D.	—	—	—	—
Kurt Von Emster	—	—	—	—
Tom Woiwode, Ph.D.	—	—	—	—
Pablo Cagnoni, M.D.(5)	$ 1,973	$357,768	$ 7,500	$367,241

(1) Amounts reported represent a prorated portion of the annual retainer each of Drs. Coles and Cagnoni earned for their board service in 2015 and, in the case of Dr. Coles, his service as chairman of our board of directors.

(2) Amount represents the aggregate grant date fair value of the option award granted to Dr. Coles in 2015 computed in accordance with FASB ASC Topic 718. Pursuant to FASB ASC Topic 718, the amount shown excludes the impact of estimated forfeitures related to service-based vesting conditions. For additional information on the valuation assumptions underlying the value of these awards, see the notes to our consolidated financial statements and discussions included elsewhere in this prospectus.

(3) Amounts reported represent fees earned for consulting services provided to us prior to appointment to our board of directors.

(4) As of December 31, 2016, Dr. Coles held an option to purchase 80,428 shares, which option vests in 48 equal monthly installments following October 9, 2015. This option accelerates in full upon a termination of Dr. Cole's service by us without cause or upon a change in control.

(5) As of December 31, 2016, Dr. Cagnoni held an option to purchase 28,150 shares, which option vests in 48 equal monthly installments following December 8, 2015. This option accelerates in full upon a termination of Dr. Cagnoni's service by us without cause or upon a change in control.

In October 2015, we entered into offer letters with each of Dr. Coles and Dr. Cagnoni to serve as members of our board of directors. Each offer letter provides for an initial option award (80,428 shares in the case of Dr. Coles and 28,150 shares in the case of Dr. Cagnoni), as well as an annual cash retainer equal to $30,000. In addition, Dr. Coles' offer letter provided him with an additional annual cash retainer equal to $20,000 in connection with his service as the chairman of our board of directors.

Equity Incentive Plans

2015 Stock Option And Grant Plan

The 2015 Stock Option and Grant Plan, or 2015 Stock Option Plan, was approved by our board of directors and our shareholders in April 2015. As of May 1, 2016, 10,067 common shares have been reserved for issuance under the 2015 Stock Option Plan in the form of incentive stock options, non-qualified stock options, restricted stock, unrestricted stock, restricted stock units or any combination of the foregoing. The shares issuable pursuant to awards granted under the 2015 Stock Option Plan are authorized but unissued shares.

The 2015 Stock Option Plan is administered by our board, or at the discretion of the board, a committee of the board comprised of not less than two (2) directors, which has full power to select the employees, directors and service providers to whom awards will be granted and to determine the specific terms and conditions of each award, subject to the provisions of the 2015 Stock Option Plan.

The option exercise price or the restricted stock purchase price of each award granted under the 2015 Stock Option Plan is determined by our board, or the designated committee, and may not be less than the fair market value of a share of common shares on the date of grant. The term of each option is fixed by the board and may not exceed 10 years from the date of grant. The board determines at what time or times each option may be exercised when granting the option.

The 2015 Stock Option Plan provides that, upon a sale transaction of the company, unless provision is made in connection with the sale transaction in the sole discretion of the parties thereto for the assumption or continuation of the awards by the successor entity or substitution of the awards with new awards of the successor entity, with appropriate adjustment, all options not exercised will terminate upon the closing of the sale transaction.

Our board may amend the 2015 Stock Option Plan but no such action may adversely affect the rights of an award holder without such holder's consent. Approval by our shareholders of amendments to the 2015 Stock Option Plan must be obtained if required by law.

As of December 31, 2015, options to purchase 581,999 common shares were outstanding under the 2015 Stock Option Plan. During the year ended December 31, 2015, we granted options to purchase 581,999 common shares under the 2015 Stock Option Plan. Our board has determined not to make any further awards under the 2015 Stock Option Plan following the completion of this offering.

2016 Stock Option Plan

On , our board of directors adopted and our shareholders approved our 2016 Stock Option and Incentive Plan, or 2016 Stock Option Plan, which will become effective upon completing of this offering and will replace the 2015 Stock Option Plan. Our 2016 Stock Option Plan provides us flexibility to use various equity-based incentive and other awards as compensation tools to motivate our workforce. These tools include stock options, stock appreciation rights, restricted stock, restricted stock units, unrestricted stock, performance share awards and cash-based awards. The 2016 Stock Option Plan will become effective immediately prior to the completion of this offering.

We have initially reserved common shares for the issuance of awards under the 2016 Stock Option Plan (not including common shares reserved for issuance under our 2016 Stock Option Plan, which will be added to the shares reserved under the 2016 Stock Option Plan), which may be increased on the first day of each fiscal year by up to % of the number of common shares issued and outstanding on the immediately preceding December 31. This number is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

The shares issuable pursuant to awards granted under the 2016 Stock Option Plan will be authorized but unissued shares or shares that we reacquire. The common shares underlying any awards from the 2016 Stock Option Plan and the 2016 Stock Option Plan that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without any issuance of common shares, expire or are otherwise terminated (other than by exercise) under the 2016 Stock Option Plan will be added back to the shares available for issuance under the 2016 Stock Option Plan.

Under the 2016 Stock Option Plan, stock options or stock appreciation rights with respect to no more than shares may be granted to any one individual in any one calendar year and the maximum aggregate number of shares that may be issued in the form of incentive stock options shall not exceed the initial number of shares reserved and available for issuance under the 2016 Stock Option Plan.

The 2016 Stock Option Plan will be administered by the compensation, nomination and corporate governance committee of the board of directors. The compensation, nomination and corporate governance committee, or compensation committee, has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, to make any combination of awards to participants, and to determine the specific terms and conditions of each award, subject to the provisions of the 2016 Stock Option Plan. Employees, nonemployee directors and other key persons (including consultants) are eligible to receive awards under the 2016 Stock Option Plan.

The 2016 Stock Option Plan permits the granting of both options to purchase common shares intended to qualify as incentive stock options under Section 422 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, and options that do not so qualify. The exercise price of each stock option will be determined by our compensation committee but may not be less than 100% of the fair market value of our common shares on the date of grant or, in the case of an incentive stock option granted to a 10% owner, less than 110% of the fair market value of our common shares on the date of grant. The term of each stock option will be fixed by the compensation committee and may not exceed 10 years from the date of grant (or five years in the case of an incentive stock option granted to a 10% owner). The compensation committee will also determine the vesting schedule for granted stock options.

The compensation committee may award stock appreciation rights subject to such conditions and restrictions as it may determine. Stock appreciation rights entitle the recipient to shares of common shares, or cash, equal to the value of the appreciation in our stock price over the exercise price. The exercise price of each stock appreciation right may not be less than 100% of the fair market value of the common shares on the date of grant.

The compensation committee may award restricted stock or restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and/or continued employment or service with us through a specified vesting period. Our compensation committee may also grant common shares that are free from any restrictions under the 2016 Stock Option Plan. Unrestricted stock may be granted to participants in recognition of past services or for other valid consideration and may be issued in lieu of cash compensation due to such participant.

The compensation committee may grant performance share awards to participants that entitle the recipient to receive share awards of common shares upon the achievement of certain performance goals and such other conditions as our compensation committee shall determine.

The compensation committee may grant performance-based awards to participants in the form of restricted stock, restricted stock units or performance shares upon the achievement of certain performance goals and such other conditions as the compensation committee shall determine. The compensation committee may grant such performance-based awards under the 2016 Stock Option Plan that are intended to qualify as “performance-based compensation” under Section 162(m) of the Code. Those awards would only vest or become payable upon the attainment of performance goals that are established by our compensation committee and related to one or more performance criteria. The performance criteria that could be used with respect to any such awards include: total

shareholder return, earnings before interest, taxes, depreciation and amortization, net income (loss) (either before or after interest, taxes, depreciation and/or amortization), changes in the market price of our common shares, economic value-added, sales or revenue, development, clinical or regulatory milestones, acquisitions or strategic transactions, operating income (loss), cash flow (including, but not limited to, operating cash flow and free cash flow), return on capital, assets, equity, or investment, return on sales, gross or net profit levels, productivity, expense, margins, operating efficiency, customer satisfaction, working capital, earnings (loss) per share, sales or market shares and number of customers, any of which may be measured either in absolute terms or as compared to any incremental increase or as compared to results of a peer group. From and after the time that we become subject to Section 162(m) of the Code, the maximum award that is intended to qualify as "performance-based compensation" under Section 162(m) of the Code that may be made to any one employee during any one calendar year period is shares with respect to a stock-based award.

The 2016 Stock Option Plan provides that upon the effectiveness of a "sale event," as defined in the 2016 Stock Option Plan, all options and stock appreciation rights that are not exercisable immediately prior to the effective time of the sale event shall become fully exercisable as of the effective time of the sale event, all other awards with time-based vesting, conditions or restrictions, shall become fully vested and nonforfeitable as of the effective time of the sale event and all awards with conditions and restrictions relating to the attainment of performance goals may become vested and nonforfeitable in the discretion of the compensation committee and all awards granted under the 2016 Stock Option Plan shall terminate. In addition, in connection with the termination of the 2016 Stock Option Plan upon a sale event, we may make or provide for a cash payment to participants holding options and stock appreciation rights equal to the difference between the per share cash consideration payable to shareholders in the sale event and the exercise price of the options or stock appreciation rights.

Our board of directors may amend or discontinue the 2016 Stock Option Plan and our compensation committee may amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose, including option repricing, but no such action may adversely affect rights under an award without the holder's consent. Certain amendments to the 2016 Stock Option Plan may require the approval of our shareholders.

No awards may be granted under the 2016 Stock Option Plan after the date that is 10 years from the date of shareholder approval of the 2016 Stock Option Plan.

2016 Employee Stock Purchase Plan

Our 2016 Employee Stock Purchase Plan was adopted by our board of directors and approved by our shareholders on , 2016 and will become effective upon completion of this offering. Our 2016 Employee Stock Purchase Plan authorizes the initial issuance of up to a total of common shares to participating employees, which may be increased on the first day of each fiscal year by up to % of the number of common shares issued and outstanding on the immediately preceding December 31. This number is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

All employees who have been employed by us or our designated subsidiaries for at least six months and whose customary employment is for more than 20 hours a week are eligible to participate in our 2016 Employee Stock Purchase Plan. Any employee who owns, or would own upon such purchase under our 2016 Employee Stock Purchase Plan, 5% or more of the voting power or value of our stock is not eligible to purchase shares under our 2016 Employee Stock Purchase Plan.

We may make one or more offerings to our employees to purchase stock under our 2016 Employee Stock Purchase Plan. Unless otherwise determined by the administrator of our 2016 Employee Stock Purchase Plan, each offering will begin on the first business day occurring on or after each January 1st and July 1st and will end on the last business day occurring on or before the following June 30th and December 31st, respectively, each referred to as offering periods. The administrator may designate different offering periods in its discretion but no offering shall exceed 12 months in duration or overlap with another offering.

Each employee who is a participant in our 2016 Employee Stock Purchase Plan may purchase shares by authorizing payroll deductions of up to 10% of his or her eligible compensation during an offering period. Unless the participating employee has previously withdrawn from the offering, his or her accumulated payroll deductions will be used to purchase common shares on the last business day of the offering period at a price equal to 85% of the fair market value of the common shares on either the first or the last day of the offering period, whichever is lower, provided that no more than 2,500 shares of common shares or such other lesser maximum number established by the plan administrator may be purchased by any one employee during each offering period. Under applicable tax rules, an employee may purchase no more than $25,000 worth of common shares, valued at the start of the purchase period, under our 2016 Employee Stock Purchase Plan in any calendar year.

The accumulated payroll deductions of any employee who is not a participant on the last day of an offering period will be refunded. An employee's rights under our 2016 Employee Stock Purchase Plan terminate upon voluntary withdrawal from the plan or when the employee ceases employment for any reason.

Our 2016 Employee Stock Purchase Plan may be terminated or amended by our board of directors at any time. Amendments that increase the number of common shares authorized under our 2016 Employee Stock Purchase Plan and certain other amendments require the approval of our shareholders.

Pension Plan

We participate in a retirement plan, or the Pension Plan, organized through enrollment in an independent collective foundation that covers our employees in Switzerland, including Dr. Novak. The assets are invested by the collective foundation in a diversified portfolio that respects the requirements of the Swiss Law on Occupational Retirement, Survivors and Disability Pension Plans, or BVG. Under the Pension Plan, both we and the employee share the costs equally. The structure of the Pension Plan and the legal provisions of the BVG mean that we are exposed to actuarial risks. The main risks are investment risk, interest risk, disability risk and the risk of longevity. Through the affiliation to a collective foundation, we have minimized these risks, since they are shared between a much greater number of participants.

The collective foundation is governed by a foundation board. The board is made up of an equal number of employee and employer representatives of the different affiliated companies. We have no direct influence on the investment strategy of the collective foundation. We cannot determine the benefits or how they are financed directly. The foundation board of the collective foundation is responsible for defining the investment strategy, for making changes to the pension fund regulations and in particular, also for defining the financing of the pension benefits.

The old age benefits are based on retirement savings for each employee, coupled with annual retirement credits and interest (there is no possibility to credit negative interest). At retirement age, the insured members can choose whether to take a pension for life, which includes a spouse's pension, or a lump sum. In addition to retirement benefits, the plan benefits also include disability and death benefits. Insured members may also buy into the scheme to improve their pension provision up to the maximum amount permitted under the rules of the plan and may withdraw funds early for the purchase of a residential property for their own use subject to limitations under Swiss law. On leaving employment with us, retirement savings are transferred to the pension institution of the new employer or to a vested benefits institution. This type of benefit may result in pension payments varying considerably between individual years. In defining the benefits, the minimum requirements of the BVG and its implementing provisions must be observed. The BVG defines the minimum pensionable salary and the minimum retirement credits. In Switzerland, the minimum interest rate applicable to these minimum retirement savings is set by the Swiss Federal Council at least once every two years. In 2015 the rate was 1.75% and for 2016 it is 1.25%.

PRINCIPAL SHAREHOLDERS

The following table presents information relating to the beneficial ownership of our common shares as of May 9, 2016, as if the conversion of our preferred shares into common shares on a one-for-one basis had occurred, by:

- each person, or group of affiliated persons, known by us to own beneficially more than 5% of our outstanding common shares;
- each of our named executive officers and directors; and
- all executive officers and directors as a group.

Upon completion of this offering, all of our outstanding preferred shares will automatically be converted into common shares on a one-for-one basis and we will have only one class of shares issued and outstanding. All holders of our common shares will have the same voting rights upon the completion of this offering.

The number of common shares beneficially owned by each entity, person, executive officer or director is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any common shares over which the individual has sole or shared voting power or investment power as well as any common shares that the individual has the right to acquire within 60 days of May 9, 2016 through the exercise of any option, warrant or other right. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all common shares held by that person.

The percentage of outstanding common shares is computed on the basis of 8,989,129 common shares outstanding as of May 9, 2016, which includes conversion of all our outstanding preferred shares on a one-for-one basis into 5,651,105 common shares. The information relating to the number and percentage of shares beneficially owned after the offering assumes the sale by us of shares of common shares in this offering and the sale of common shares in the concurrent private placement. Common shares that a person has the right to acquire within 60 days of May 9, 2016 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all named executive officers and directors as a group. Unless otherwise indicated below, the address for each beneficial owner is CRISPR Therapeutics AG, Aeschenvorstadt 36, 4051 Basel, Switzerland.

	Shares Beneficially Owned Before This Offering and the Concurrent Private Placement		Shares Beneficially Owned After This Offering and the Concurrent Private Placement	
Shareholder	Number	Percent	Number	Percent
5% Shareholders				
Abingworth Bioventures VI, L.P.(1)	763,744	8.50%		
Bayer Global Investments B.V.(2)	781,599	8.69%		
Celgene Alpine Investment Company III, LLC(3)	1,210,449	13.47%		
Entities affiliated with New Enterprise Associates(4)	946,268	10.53%		
Entities affiliated with Versant Ventures(5)	2,024,503	22.52%		
S.R. One, Limited(6).	946,238	10.53%		
Vertex Pharmaceuticals (Europe) Limited(7)	673,016	7.49%		
Named Executive Officers and Directors				
Rodger Novak, M.D.(8)	426,883	4.73%		
Sven Ante (Bill) Lundberg, M.D.(9)	151,565	1.69%		
Samarth Kulkarni, Ph.D.(10)	40,214	*		
N. Anthony Coles, M.D.(11)	15,080	*		
Bradley Bolzon, Ph.D.(12)	2,077,903	23.12%		
Ali Behbahani, M.D.	—	*		

Shareholder	Shares Beneficially Owned Before This Offering and the Concurrent Private Placement		Shares Beneficially Owned After This Offering and the Concurrent Private Placement	
	Number	Percent	Number	Percent
Kurt von Emster(13)	763,744	8.50%		
Simeon J. George, M.D.(14)	946,238	10.53%		
Thomas Woiwode, Ph.D.(15)	2,077,903	23.12%		
Pablo Cagnoni, M.D.	—	*		
All executive officers and directors as a group (11 persons)	4,536,588	50.13%		

* Indicates beneficial ownership of less than 1% of the total issued and outstanding common shares.

(1) Consists of (a) 706,215 common shares issuable upon conversion of Series A-3 Preferred Shares and (b) 57,529 common shares issuable upon conversion of Series B Preferred Shares beneficially owned Abingworth Bioventures VI, L.P, or ABV VI. Abingworth Bioventures VI GP LP, a Scottish limited partnership, serves as the general partner of ABV VI. Abingworth General Partner VI LLP, an English limited liability partnership, serves as the general partner of Abingworth Bioventures VI GP LP. ABV VI (acting by its general partner Abingworth Bioventures VI GP LP, acting by its general partner Abingworth General Partner VI LLP) has delegated to Abingworth LLP, an English limited liability partnership, all investment and dispositive power over the securities held by ABV VI. An investment committee of Abingworth LLP, comprised of Stephen W. Bunting, Timothy Haines, Kurt von Emster and Genghis Lloyd-Harris, approves investment and voting decisions by a majority vote, and no individual member has the sole control or voting power over the securities held by ABV VI. Mr. von Emster is a Managing Partner of Abingworth LLP and a member of our board of directors. Each of Abingworth Bioventures VI GP LP, Abingworth General Partner VI LLP, Mr. von Emster, Dr. Bunting, Dr. Haines and Dr. Lloyd-Harris disclaims beneficial ownership of these shares, except to the extent of their pecuniary interest in such shares. The principal address for each of the entities and individuals listed above is c/o Abingworth LLP, Princes House, 38 Jermyn Street, London, England SW1Y 6DN.

(2) Consists of 781,559 common shares issuable upon conversion of Series B Preferred Shares beneficially owned Bayer Global Investments B.V., a wholly owned subsidiary of Bayer AG. Bayer AG has the power to vote, acquire, hold and dispose of all such shares. Bayer AG disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. The address for Bayer AG is 51368 Leverkusen, Germany.

(3) Consists of 1,210,449 common shares issuable upon conversion of Series B Preferred Shares beneficially owned Celgene Alpine Investment Company III, LLC, a wholly owned subsidiary of Celgene Corporation, or Celgene. Celgene has the power to vote, acquire, hold and dispose of all such shares. Celgene disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. The principal address for Celgene is 86 Morris Avenue, Summit, New Jersey 07901.

(4) Consists of (a) 881,356 common shares issuable upon conversion of Series A-3 Preferred Shares and 63,500 common shares issuable upon conversion of Series B Preferred Shares beneficially owned by New Enterprise Associates 15, L.P., or NEA 15, and (b) 1,412 common shares issuable upon conversion of Series A-3 Preferred Shares beneficially owned by NEA Ventures 2015, L.P., or NEA Ventures. The shares directly held by NEA 15 are indirectly held by NEA Partners 15, L.P., or NEA Partners 15, the sole general partner of NEA 15, NEA 15 GP, LLC, or NEA 15 LLC, the sole general partner of NEA Partners 15 and each of the individual managers of NEA 15 LLC. The individual managers, or collectively, the managers, of NEA 15 LLC are Peter J. Barris, Forest Baskett, Anthony A Florence, Jr., Krishna “Kittu” Kolluri, David M. Mott, Scott D. Sandell, Peter Sonsini, Ravi Viswanathan, Jon Sakoda and Harry R. Weller. The managers share voting and dispositive power with regard to the shares held by NEA 15. Karen P. Welsh, the general partner of NEA Ventures, shares voting and dispositive power with regard to the shares held by NEA Ventures. Dr. Behbahani, a member of our board of directors, has no dispositive power with regard to any shares held by NEA 15 and NEA Ventures. Each of the managers, Karen P. Welsh and Dr. Behbahani, disclaim beneficial ownership of all applicable shares except to the extent of their actual pecuniary interest in such shares. The principal address for NEA 15 and NEA Ventures is c/o New Enterprise Associates, Inc., 1954 Greenspring Drive, Suite 600, Timonium, Maryland 21093.

(5) Consists of (a) 131,174 common shares issuable upon conversion of Series A-1 Preferred Shares, 930,143 common shares issuable upon conversion of Series A-2 Preferred Shares, 69,323 common shares issuable upon conversion of Series B Preferred Shares and 71,895 common shares beneficially owned by Versant Venture Capital IV, L.P., or VVC IV, (b) 826 common shares issuable upon conversion of Series A-1 Preferred Shares, 5,857 common shares issuable upon conversion of Series A-2 Preferred Shares and 436 common shares issuable upon conversion of Series B Preferred Shares beneficially owned by Versant Side Fund IV, L.P., or VSF IV, (c) 663,125 common shares issuable upon conversion of Series A-3 Preferred Shares and 51,950 common shares issuable upon conversion of Series B Preferred Shares beneficially owned by Versant Venture Capital V, L.P., or VVC V, (d) 19,947 common shares issuable upon conversion of Series A-3 Preferred Shares and 1,563 common shares issuable upon conversion of Series B Preferred Shares beneficially owned by Versant Affiliates Fund V, L.P., or VAF V, (e) 50,467 common shares issuable upon conversion of Series A-3 Preferred Shares and 3,954 common shares issuable upon conversion of Series B Preferred Shares beneficially owned by Versant Venture Capital V (Canada) LP, or VVC CAN, and (f) 22,111 common shares issuable upon conversion of Series A-3 Preferred Shares and 1,732 common shares issuable upon conversion of Series B Preferred Shares beneficially owned by Versant Ophthalmic Affiliates Fund I, L.P, or VOA. Versant Ventures IV, LLC, or VV IV, serves as the sole general partner of VVC IV and VSF IV and owns no shares directly. Brian G. Atwood, Samuel D. Colella, Ross A. Jaffe, William J. Link, Rebecca B. Robertson, Bradley Bolzon, Ph.D., Charles M. Warden, Kirk G. Nielsen, Thomas Woiwode and Robin L. Praeger are managing directors of VV IV and share voting and dispositive power over the shares held by VVC IV and VSF IV; however, they each disclaim beneficial ownership of the shares held by VVC IV and VSF IV, except to the extent of their pecuniary interests therein. Versant Ventures V, LLC, or VV V, serves as the sole general partner of VOA, VAF V and VVC V and owns no shares directly. Versant Ventures V (Canada) GP-GP, Inc. or VV V CAN GP, serves as the sole general partner of Versant Ventures V (Canada), L.P., or VV V CAN, which serves as the sole general partner of VVC CAN and owns no shares directly. Samuel D. Colella, William J. Link, Bradley Bolzon, Ph.D., Robin L. Praeger, Kirk G. Nielson and Thomas Woiwode, Ph.D. are managing directors of VV V and directors of VV V CAN and share voting and dispositive power over the shares held by VOA, VAF V, VVC V and VVC CAN; however, they each disclaim beneficial ownership of the shares held by VOA, VAF V, VVC V and VVC CAN, except to the extent of their pecuniary interests therein. Drs. Bolzon and Woiwode are members of our board of directors. The address for each of the Versant Ventures entities is One Sansome Street, Suite 3630, San Francisco, CA 94104.

(6) Consists of (a) 882,768 common shares issuable upon conversion of Series A-3 Preferred Shares and (b) 63,470 common shares issuable upon conversion of Series B Preferred Shares beneficially owned by S.R. One Limited. S.R. One, Limited is an indirect, wholly-owned subsidiary of GlaxoSmithKline plc. Dr. George is a partner a S.R. One, Limited and a member of our board of directors. Dr. George disclaims beneficial ownership of these shares, except to the extent of his pecuniary interest therein. The principal address for S.R. One, Limited is S.R. One, Limited is 161 Washington Street, Suite 500, Conshohocken, Pennsylvania 19428.

(7) Consists of 673,016 common shares issuable upon conversion of Series B Preferred Shares beneficially owned Vertex Pharmaceuticals (Europe) Limited. Vertex Pharmaceutical (Europe) Limited is a wholly owned subsidiary of Vertex Pharmaceuticals, Incorporated. The principal place of business Vertex Pharmaceuticals, Incorporated is 50 Northern Avenue, Boston, Massachusetts 02210.

(8) Consists of (a) 292,382 common shares owned directly and (b) 89,261 common shares owned indirectly and (c) 45,240 common shares issuable upon exercise of stock options granted to Dr. Novak that are exercisable within 60 days of May 9, 2016.

(9) Consists of (a) 16,565 common shares issuable upon conversion of Series B Preferred Shares and (b) 135,000 restricted common shares issued to Dr. Lundberg that vest within 60 days of May 9, 2016.

(10) Consists of 40,214 restricted common shares

(11) Consists of 15,080 common shares issuable upon exercise of stock options granted to Dr. Coles that are exercisable within 60 days of May 9, 2016.

(12) Consists of (a) the shares disclosed in footnote (5) above and (b) 53,400 common shares. Dr. Bolzon is a managing director of VV IV, VV V and VV V CAN. Dr. Bolzon disclaims beneficial ownership of the shares held by VVC IV, VSF IV, VOA, VAF V, VVC V and VVC CAN, except to the extent of his pecuniary interests therein.

(13) Consists of the shares disclosed in footnote (1) above. Mr. von Emster is a Managing Partner of Abingworth LLP. Mr. von Emster disclaims beneficial ownership of the shares held by Abingworth Bioventures VI, L.P., except to the extent of his pecuniary interest therein.

(14) Consists of the shares disclosed in footnote (6) above. Dr. George is a partner at S.R. One, Limited. Dr. George has no dispositive power with regard to any shares held by S.R. One, Limited and disclaims beneficial ownership of the shares held by S.R. One Limited, except to the extent of his pecuniary interest in such shares.

(15) Consists of (a) the shares disclosed in footnote (5) above and (b) 53,400 common shares. Dr. Woiwode is a managing director of VV IV, VV V and VV V CAN. Dr. Woiwode disclaims beneficial ownership of the shares held by VVC IV, VSF IV, VOA, VAF V, VVC V and VVC CAN, except to the extent of his pecuniary interests therein.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a description of related party transactions we have entered into since our inception in October 2013 with any of our executive officers, directors and holders of more than 5% of any class of our voting securities, or any member of the immediate family of any of the foregoing persons, other than the compensation arrangements we describe under "Management."

Shareholders' Agreement

We have entered into a shareholders' agreement with all of our shareholders, which provides our shareholders with certain board nomination rights, preemptive rights, drag-along rights, tag-along rights and registration rights. Pursuant to the shareholders' agreement, each of S.R. One, Limited, NEA and Abingworth Bioventures VI, L.P. has the right to designate one director to our board of directors and entities affiliated with Versant Ventures have the right to designate two directors to our board of directors. S.R. One, Limited, NEA and Abingworth Bioventures VI, L.P. have designated Dr. George, Dr. Behbahani and Mr. von Emster, respectively. Versant has designated Drs. Bolzon and Woiwode. Other than the registration rights discussed under "Common Shares Eligible for Future Sale – Shareholder Registration Rights," the shareholders' agreement will terminate in connection with this offering.

Pursuant to our shareholders' agreement, we have agreed to consult with our U.S. tax advisors to determine whether we would be treated as a controlled foreign corporation, or CFC, or a passive foreign investment company, or PFIC, for each tax year. If we are a CFC for a taxable year, we are generally required to advance pay to certain U.S. shareholders an amount equal to 50% of our undistributed earnings included in the gross income of such shareholder pursuant to Section 951 of the U.S. Internal Revenue Code of 1986, as amended, or the Code. If we are a PFIC for a taxable year, we are generally required to advance pay to certain U.S. shareholders who make a qualified electing fund election, or QEF election, an amount equal to 50% of the amount that such shareholder is required to include in gross income pursuant to Section 1293 of the Code. All such amounts shall be deemed an advance against the payment of any future dividends or distributions. We also have obligations to provide timely notice and other information to certain of our U.S. shareholders regarding the determination of, and our status of, a CFC and PFIC. For the year ended December 31, 2015, we have determined that we are both a CFC and a PFIC. The obligation to make advance payments under the shareholders' agreement will terminate upon the closing of an IPO (as defined in the shareholders' agreement).

Equity Financings

Series A-1 Financing

In October 2013, we issued and sold an aggregate of 132,000 Series A-1 Preferred Shares at a purchase price of CHF 3.80 per share to entities affiliated with Versant Ventures for gross proceeds of CHF 0.5 million. Entities affiliated with Versant Ventures hold greater than 5% of our voting securities and are affiliated with Bradley Bolzon, Ph.D. and Thomas Woiwode, Ph.D., both members of our board of directors.

Common Share Issuance

Simultaneously with the issuance of the Series A-1 Preferred Shares, we issued 100,500 common shares to entities affiliated with Versant at a nominal value per share, for aggregate proceeds of CHF 10,050.

Series A-2 Financing

In April 2014, we issued an aggregate of 936,000 Series A-2 Preferred Shares at a purchase price of CHF 10.162 per share to entities affiliated with Versant Ventures, whereby CHF 4.82 per share was received upon issuance, resulting in gross proceeds of CHF 4.5 million. The balance of CHF 5.342 per share was called in February 2015 by our board of directors, resulting in additional gross proceeds of CHF 5.0 million. Entities affiliated with Versant Ventures hold greater than 5% of our voting securities and are affiliated with Bradley Bolzon, Ph.D. and Thomas Woiwode, Ph.D., both members of our board of directors.

Series A-3 Financing

In April 2015, we issued an aggregate of 3,227,401 Series A-3 Preferred Shares at a purchase price of $14.16 per share, whereby $7.08 per share was received upon issuance, resulting in gross proceeds of approximately $22.8 million. The balance of $7.08 per share was called in May 2016 by our board of directors upon the satisfaction of the conditions set forth in the purchase agreement. When received, this will result in additional gross proceeds of approximately $22.8 million. The table below sets forth the aggregate number and purchase price of Series A-3 Preferred Shares issued to our directors or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof:

Name	Shares	Aggregate Purchase Price
Entities affiliated with Versant Ventures(1)	755,650	$ 10,700,004
S.R. One, Limited(2)	882,768	12,499,995
Entities affiliates with NEA Enterprise Associates(3)	882,768	12,499,995
Abingworth Bioventures VI, L.P.(4)	706,215	10,000,004
Total:	3,227,401	$ 45,699,998

(1) Entities affiliated with Versant Ventures hold greater than 5% of our voting securities and are affiliated with Bradley Bolzon, Ph.D. and Thomas Woiwode, Ph.D., both members of our board of directors.
(2) S.R. One, Limited holds greater than 5% of our voting securities and is affiliated with Simeon J. George, M.D., a member of our board of directors.
(3) Entities affiliated with NEA Enterprise Associates hold greater than 5% of our voting securities and are affiliated with Ali Behbahani, M.D., a member of our board of directors.
(4) Abingworth Bioventures VI, L.P. holds greater than 5% of our voting securities and is affiliated with Kurt von Emster, a member of our board of directors.

Series B Financing

In May 2015, we issued an aggregate of 1,355,704 Series B Preferred Shares at a purchase price of CHF 20.6535 per share for gross proceeds of approximately CHF 28.0 million.

The table below sets forth the aggregate number of Series B Preferred Shares issued to our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, in the May 2015 closing:

Name	Shares	Aggregate Purchase Price
Entities affiliated with Versant Ventures(1)	61,670	CHF 1,273,701
S.R. One, Limited(2)	29,852	616,548
NEA Ventures 2015, Limited Partnership(3)	29,852	616,548
Abingworth Bioventures VI, L.P.(4)	23,881	493,226
Celgene Alpine Investment Company III, LLC	1,210,449	25,000,008
Total:	1,335,704	CHF 28,000,033

(1) Entities affiliated with Versant Ventures hold greater than 5% of our voting securities and are affiliated with Bradley Bolzon, Ph.D. and Thomas Woiwode, Ph.D., both members of our board of directors.
(2) S.R. One, Limited holds greater than 5% of our voting securities and is affiliated with Simeon J. George, M.D., a member of our board of directors.
(3) NEA Ventures 2015, Limited Partnership is affiliated with Ali Behbahani, M.D., a member of our board of directors.
(4) Abingworth Bioventures VI, L.P. holds greater than 5% of our voting securities and is affiliated with Kurt von Emster, a member of our board of directors.

Series B Conversion

In October 2015, we entered into a Convertible Loan Agreement with Vertex Pharmaceuticals (Europe) Limited pursuant to which it made an investment of $30.0 million. Additionally, in December 2015, we entered into a Convertible Loan Agreement with Bayer Global Investments B.V., or Bayer BV, pursuant to which Bayer BV made an investment of $35.0 million. In connection with each loan agreement, pursuant to Swiss Law, all of our then current shareholders were allowed to participate as additional lenders in each loan agreement on a pro-rata basis to their respective shareholdings.

The outstanding principal balance together with accrued interest thereon under each loan agreement was converted into Series B Preferred Shares in January 2016 at a conversion price of $44.78 per share. The table below sets forth the aggregate number of Series B Preferred Shares issued upon conversion to our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, in the January 2016 conversion:

Name	Aggregate Principal Amount of Loans	Series B Shares Received Upon Conversion
Entities affiliated with Versant Ventures(1)	$ 3,000,000	67,288
S.R. One, Limited(2)	1,500,000	33,618
New Enterprise Associates 15, L.P.(3)	1,500,000	33,648
Abingworth Bioventures VI L.P.(4)	1,500,000	33,648
Vertex Pharmaceuticals (Europe) Limited	30,000,000	673,016
Bayer Global Investments B.V.	35,000,000	781,599
Sven Ante (Bill) Lundberg, M.D.	738,450	16,565
Total:	$ 73,238,450	1,639,382

(1) Entities affiliated with Versant Ventures hold greater than 5% of our voting securities and are affiliated with Bradley Bolzon, Ph.D. and Thomas Woiwode, Ph.D., both members of our board of directors.
(2) S.R. One, Limited is affiliated with Simeon J. George, M.D., a member of our board of directors.
(3) New Enterprise Associates 15, L.P. is affiliated with Ali Behbahani, M.D., a member of our board of directors.
(4) Abingworth Bioventures VI, L.P. is affiliated with Kurt von Emster, a member of our board of directors.

Share Exchange

In March 2015, we acquired 4,600 ordinary shares of our subsidiary, TRACR Hematology Limited, or TRACR, representing 82.1% of the ordinary share capital, pursuant to a share exchange transaction with the shareholders of TRACR, which we refer to as the share exchange. In exchange for the 4,600 ordinary shares of TRACR and the assignment of certain rights to subscribe for ordinary shares of TRACR, we issued an aggregate of 452,663 of our common shares and restricted common shares to the founders, employees and non-employee advisors of TRACR, including (i) 157,449 unrestricted common shares to Rodger Novak, our Chief Executive Officer and one of the co-founders of TRACR, and (ii) 98,405 unrestricted common shares to Shaun Foy, our then Chief Financial Officer and one of the co-founders of TRACR.

Bayer Joint Venture

In December 2015, we entered into a Joint Venture Agreement, or the JV Agreement, with Bayer HealthCare LLC, or Bayer Healthcare, to create Casebia Therapeutics LLP, or Casebia, to discover, develop and commercialize new therapeutics. At the closing of the JV Agreement in March 2016, we contributed $0.1 million to Casebia and Bayer Healthcare contributed an initial amount of $45 million. Bayer Healthcare is committed to contribute up to $300 million in the aggregate, including the $45 million initial contribution. Additionally, as part of our contribution to Casebia, in March 2016, we entered into a IP Contribution Agreement, or the CRISPR IP

Contribution Agreement, with Casebia. Pursuant to the CRISPR IP Contribution Agreement, we granted Casebia an exclusive, worldwide, fully paid-up, royalty-free license, including the right to sublicense, to the use of our CRISPR/Cas9 technology. In return, Casebia is required to pay us an aggregate amount of $35 million. For a more detailed description of our joint venture with Bayer Healthcare, see "Business – Bayer Joint Venture."

Bayer Subscription Agreement

In connection with the JV Agreement, in December 2015, we entered in a subscription agreement, or the Subscription Agreement, with Bayer Global Investments B.V., or Bayer BV. Pursuant to the Subscription Agreement, Bayer BV was given the option, at its election, to purchase up to $35 million of our common shares in a private placement concurrent with this offering at a per share price equal to the public offering price of this offering. In April 2016, Bayer BV provided us written notice of its exercise of the option. We may reduce the amount of Bayer BV's purchase in our sole discretion, subject to the terms of the Subscription Agreement.

Vertex Collaboration Agreement

In October 2015, we entered into a Strategic Collaboration, Option and License Agreement, or the Collaboration Agreement, with Vertex Pharmaceuticals, Incorporated and Vertex Pharmaceuticals (Europe) Limited, together referred to as Vertex. Pursuant to the Collaboration Agreement, we will provide technology and options to obtain licenses relating to our CRISPR/Cas9 technology. In exchange, we received a $105 million up front payment from Vertex, which was comprised of $75 million in cash and a $30 million equity investment in the form of the Vertex Convertible Loan. The Vertex Convertible Loan converted into Series B Preferred Shares in January 2016 as described under "*Series B Conversion*" above. Additionally, for a maximum of six collaboration targets in-licensed for development by Vertex under the Collaboration Agreement, Vertex will pay future development, regulatory and sales milestones of up to $420 million as well as royalty payments in the single digits to low teens on future sales of a commercialized product candidate. The milestone and royalty payments are each subject to reduction under certain specified conditions set forth in the Collaboration Agreement. For a more detailed description of our collaboration with Vertex, see "Business — Vertex Collaboration Agreement."

Lease with Versant Ventures

In October 2013, we moved into our principal executive offices in Switzerland. The office space is owned by Versant Ventures, an entity which holds greater than 5% of our voting securities and is affiliated with Bradley Bolzon, Ph.D. and Thomas Woiwode, Ph.D., who are members of our board of directors. We currently do not pay any lease fees for the use of the office space and we do not have a written agreement with Versant Ventures to specify the terms of our occupation. We are in the process of finalizing a formal lease with Versant Ventures.

Real Estate License Agreement with Mass Innovation Labs, LLC

In April 2015, we entered into a real estate license agreement with Mass Innovation Labs, LLC, or Mass Innovation, for office and laboratory space in Cambridge, Massachusetts. Mass Innovation leases the facility from Vertex, which holds 673,016, or approximately 7.5%, of our common shares. The fee owed each month is composed of a base license fee plus an additional membership fee based on the number of occupants at the facility during the applicable calendar month. During 2015, we paid approximately $1.0 million to Mass Innovation under the agreement.

Executive Officer and Director Compensation

See the section titled "Executive Compensation" for information regarding compensation of our executive officers and directors.

Employment Agreements

We have entered into offer letters or employment agreements with our executive officers. For more information regarding our agreements with our named executive officers for the fiscal year ended December 31, 2015, see the section titled "Executive Compensation—Narrative to Summary Compensation Table—Employment Arrangements with our Named Executive Officers."

Indemnification Agreements

We have entered into or plan to enter into indemnification agreements with each of our directors and officers, the form of which is attached as an exhibit to the registration statement of which this prospectus is a part.

Related-Party Transaction Policy

We intend to adopt a formal written policy that our executive officers, directors, holders of more than 5% of any class of our voting securities, and any member of the immediate family of and any entity affiliated with any of the foregoing persons, are not permitted to enter into a related-party transaction with us without the prior consent of our audit and finance committee, or other independent members of our board of directors in the event it is inappropriate for our audit and finance committee to review such transaction due to a conflict of interest. Any request for us to enter into a transaction with an executive officer, director, holders of more than 5% of any class of our voting securities, or any of their immediate family members or affiliates, in which the amount involved exceeds $120,000 must first be presented to our audit and finance committee for review, consideration and approval. In approving or rejecting any such proposal, our audit and finance committee will consider the relevant facts and circumstances available and deemed relevant to our audit and finance committee, including, but not limited to, whether the transaction will be on terms no less favorable than terms generally available to an unaffiliated third-party under the same or similar circumstances and the extent of the related-party's interest in the transaction. All of the transactions described in this section were entered into prior to the adoption of this policy.

DESCRIPTION OF SHARE CAPITAL AND ARTICLES OF ASSOCIATION

The Company

We are a Swiss stock corporation *(Aktiengesellschaft)* organized under the laws of Switzerland. We were incorporated on October 31, 2013. Our domicile and registered office is in Basel, Switzerland. Our head office is currently located at Aeschenvorstadt 36, 4051 Basel, Switzerland.

Share Capital

As of the date of this prospectus, our share capital is divided into common shares and four categories of preferred shares. Conditional upon the closing of this offering, all of our preferred shares will be converted into common shares on a one-for-one basis, effective upon the registration of the revised articles of association with the commercial register of the Canton of Basel-Stadt, Switzerland. See "—Articles of Association." Upon the closing of this offering, giving effect to (i) the issuance of the common shares to be sold in this offering, (ii) the conversion of all 7,290,487 of our outstanding preferred shares into common shares on a one-for-one basis, (iii) the issuance of 98,405 common shares to Dr. Emmanuelle Charpentier immediately prior to the closing of this offering pursuant to a call option agreement, dated March 20, 2015, between us and Dr. Charpentier, and (iv) our planned share split, our issued fully paid-in share capital will consist of CHF divided into common shares with a nominal value of CHF each and no preferred shares.

As of May 9, 2016, 9,087,534 of our common shares were outstanding and held by 29 shareholders of record. This amount assumes (i) the conversion of all 7,290,487 of our outstanding preferred shares into common shares on a one-for-one basis immediately prior to the closing of this offering and (ii) the issuance of 98,405 common shares to Dr. Emmanuelle Charpentier immediately prior to the closing of this offering pursuant to the Call Option Agreement.

Articles of Association

Prior to the closing of this offering, we intend to adopt amended and restated articles of association which will become effective upon the closing of this offering and the registration of the revised articles of association with the commercial register of the Canton of Basel-Stadt, Switzerland. When we refer to our articles of association in this prospectus, we refer to our amended and restated articles of association as they will be in force upon the closing of this offering.

Ordinary Capital Increase, Authorized And Conditional Share Capital

Under Swiss law, we may increase our share capital (*Aktienkapital*) with a resolution of the general meeting of shareholders (ordinary capital increase) that must be carried out by the board of directors within three months of the general meeting in order to become effective. Under our articles of association, in the case of subscription and increase against payment of contributions in cash, a resolution passed by a simple majority of the shares represented at the general meeting of shareholders regardless of abstentions or empty or invalid votes is required. In the case of subscription and increase against contributions in kind or to fund acquisitions in kind, when shareholders' statutory pre-emptive rights are withdrawn or where transformation of reserves into share capital is involved, a resolution passed by two-thirds of the shares represented at a general meeting of shareholders and the absolute majority of the nominal amount of the shares represented is required.

Furthermore, under the Swiss Code of Obligations, or the CO, our shareholders, by a resolution passed by two-thirds of the shares represented at a general meeting of shareholders and the absolute majority of the nominal amount of the shares represented, may empower our board of directors to issue shares of a specific aggregate nominal amount up to a maximum of 50% of the share capital in the form of:

- conditional capital (*bedingtes Kapital*) for the purpose of issuing shares in connection with, among other things, (i) option and conversion rights granted in connection with convertible bonds of the Company or

one of our subsidiaries or (ii) grants of rights to employees, members of our board of directors or consultants of the Company or of one of our subsidiaries or other persons providing services to the Company or a subsidiary to subscribe for new shares (conversion or option rights); or

- authorized capital (*genehmigtes Kapital*) to be utilized by the board of directors within a period determined by the shareholders but not exceeding two years from the date of the shareholder approval.

Pre-Emptive Rights

Pursuant to the CO, shareholders have pre-emptive rights *(Bezugsrechte)* to subscribe for new issuances of shares. With respect to conditional capital in connection with the issuance of conversion rights, convertible bonds or similar debt instruments, shareholders have advance subscription rights *(Vorwegzeichnungsrechte)* for the subscription of conversion rights, convertible bonds or similar debt instruments.

A resolution passed at a general meeting of shareholders by two-thirds of the shares represented and the absolute majority of the nominal value of the shares represented may authorize our board of directors to withdraw or limit pre-emptive rights or advance subscription rights in certain circumstances.

If pre-emptive rights are granted, but not exercised, the board of directors may allocate the pre-emptive rights as it elects.

With respect to our authorized share capital, the board of directors is authorized by our articles of association to withdraw or to limit the pre-emptive rights of shareholders, and to allocate them to third parties or to us, in the event that the newly issued shares are used for the following purposes:

- if the issue price of the new registered shares is determined by reference to the market price;
- for the acquisition of an enterprise, part(s) of an enterprise or participations, or for the financing or refinancing of any of such transactions, or in the event of share placement for the financing or refinancing of such transactions;
- for purposes of broadening the shareholder constituency of the Company in certain financial or investor markets, for purposes of the participation of strategic partners, or in connection with the listing or registration of new registered shares on domestic or foreign stock exchanges;
- for purposes of granting an over-allotment option of up to 20% of the total number of registered shares in a placement or sale of registered shares to the respective initial purchaser(s) or underwriter(s);
- for raising of capital (including private placements) in a fast and flexible manner which probably could not be reached without the exclusion of the statutory pre-emptive right of the existing shareholders;
- following a shareholder or a group of shareholders acting in concert having accumulated shareholdings in excess of 15% of the share capital registered in the commercial register without having submitted to the other shareholders a takeover offer recommended by the board of directors, or for the defense of an actual, threatened or potential takeover bid, in relation to which the board of directors, upon consultation with an independent financial adviser retained by it, has not recommended to the shareholders acceptance on the basis that the board of directors has not found the takeover bid to be financially fair to the shareholders; or
- for other valid grounds in the sense of Article 652b para. 2 of the CO.

Our Authorized Share Capital

Under our articles of association, our board of directors is authorized at any time until , 2016 to increase our share capital by a maximum aggregate amount of CHF through the issuance of not more than shares, which would have to be fully paid-in, with a nominal value of CHF each.

Increases in partial amounts are permitted. The board of directors has the power to determine the type of contributions, the issue price and the date on which the dividend entitlement starts.

Our board of directors is also authorized to withdraw or limit pre-emptive rights as described above. This authorization is exclusively linked to the particular available authorized share capital set out in the respective article. If the period to increase the share capital lapses without having been used by the board of directors, the authorization to withdraw or to limit the pre-emptive rights lapses simultaneously with such capital.

Our common shares to be sold in this offering will be issued out of our authorized share capital. Accordingly, upon the consummation of this offering, our authorized but unissued share capital will decrease by the amount of CHF (or by a larger amount, to the extent that any over-allotment shares will be issued).

Our Conditional Share Capital

Conditional Share Capital for Bonds and Similar Debt Instruments

Our share capital may be increased by a maximum aggregate amount of CHF through the issuance of not more than common shares, which would have to be fully paid-in, with a nominal value of CHF each, by the exercise of conversion and/or option or warrant rights granted in connection with bonds or similar instruments of the Company or one of our subsidiaries, including convertible debt instruments. Shareholders will not have pre-emptive rights in such circumstances. The holders of convertible bonds are entitled to the new shares upon the occurrence of the applicable conversion feature.

When issuing convertible bonds, the board of directors is authorized to withdraw or to limit the advance right of shareholders to subscribe to the convertible bond issuance:

- for the purpose of financing or refinancing the acquisition of enterprises, divisions thereof, or of participations or of newly planned investments of the Company; or
- if the issuance occurs in domestic or international capital markets including private placements.

To the extent that the advance subscription rights are withdrawn, (i) the instruments are to be issued at market conditions; (ii) the term to exercise the option or conversion rights may not exceed 10 years as of the date of the issuance for warrants and twenty years for conversion rights; and (iii) the exercise price for the new shares must at least correspond to the market conditions at the time of the issuance of the instruments.

Conditional Share Capital for Employee Benefit Plans

Our share capital may, to the exclusion of the pre-emptive rights of shareholders, be increased by a maximum aggregate amount of CHF through the issuance of not more than common shares, which would have to be fully paid-in, with a nominal value of CHF each, by the exercise of option or conversion rights that have been granted to employees, members of the board of directors or consultants of the Company or of one of our subsidiaries or other persons providing services to the Company or a subsidiary through one or more employee benefit plans created by the board of directors.

Uncertificated Securities

Our shares are uncertificated securities *(Wertrechte*, within the meaning of art. 973c of the CO) and, when administered by a financial intermediary *(Verwahrungsstelle*, within the meaning of the Federal Act on Intermediated Securities, "FISA"), qualify as intermediated securities *(Bucheffekten*, within the meaning of the FISA). In accordance with art. 973c of the CO, we will maintain a non-public register of uncertificated securities *(Wertrechtebuch)*. We may at any time convert uncertificated securities into share certificates (including global

certificates), one kind of certificate into another, or share certificates (including global certificates) into uncertificated securities. Following entry in the share register, a shareholder may at any time request from us a written confirmation in respect of the shares. Shareholders are not entitled, however, to request the printing and delivery of certificates. We may print and deliver certificates for shares at any time.

General Meeting Of Shareholders

Ordinary/Extraordinary Meetings, Powers

The general meeting of shareholders is our supreme corporate body. Under Swiss law, ordinary and extraordinary general meetings of shareholders may be held. Under Swiss law, an ordinary general meeting of shareholders must be held annually within six months after the end of a corporation's financial year. In our case, this means within six months after December 31 or before June 30.

The following powers are vested exclusively in the general meeting of shareholders:

- adopting and amending the articles of association, including change of a company's purpose or domicile;
- electing the members of the board of directors, the chairman of the board of directors, the members of the compensation, nomination and corporate governance committee, the auditors and the independent proxy;
- approving the annual report, the annual statutory financial statements and (to the extent required) the consolidated financial statements, and deciding on the allocation of profits as shown on the balance sheet, in particular with regard to dividends;
- approving the compensation (basis, bonus and equity) of members of the board of directors and executive management, which under Swiss law is not necessarily limited to the executive officers;
- discharging the members of the board of directors and executive management from liability with respect to their tenure in the previous financial year;
- dissolving a company with or without liquidation by corporate resolution; and
- deciding matters reserved to the general meeting of shareholders by law or the articles of association or presented to it by the board of directors.

An extraordinary general meeting of shareholders may be called by a resolution of the board of directors or, under certain circumstances, by a company's auditor, liquidator or the representatives of convertible bond holders, if any. In addition, the board of directors is required to convene an extraordinary general meeting of shareholders if shareholders representing at least 10% of the share capital request such general meeting of shareholders in writing. Such request must set forth the items to be discussed and the proposals to be acted upon. The board of directors must convene an extraordinary general meeting of shareholders and propose financial restructuring measures if, based on a company's stand-alone annual statutory balance sheet, half of the share capital and reserves are not covered by its assets.

Voting And Quorum Requirements

Shareholder resolutions and elections (including elections of members of the board of directors) require the affirmative vote of the simple majority of shares represented at the general meeting of shareholders regardless of abstentions or empty or invalid votes, unless otherwise stipulated by law.

A resolution of the general meeting of the shareholders passed by two-thirds of the shares represented at the meeting, and the absolute majority of the nominal value of the shares represented is required for:

- amending a company's corporate purpose;
- the introduction of shares with preferential voting rights;

- cancelling or amending the transfer restrictions of shares;
- creating authorized or conditional share capital;
- increasing the share capital out of equity, against contributions in-kind or for the purpose of acquiring specific assets and granting specific benefits;
- limiting or suppressing shareholder's pre-emptive rights;
- changing a company's domicile;
- alleviating or withdrawing of restrictions upon the transfer of registered shares and the removal of the voting cap of 15%;
- removing the indemnification provision for the board of directors and executive management;
- converting registered shares into bearer shares and vice versa; and
- dissolving or liquidating a company.

The same voting requirements apply to resolutions regarding transactions among corporations based on Switzerland's Federal Act on Mergers, Demergers, Transformations and the Transfer of Assets, or the Merger Act (including a merger, demerger or conversion of a corporation) see "—Compulsory Acquisitions; Appraisal Rights."

In accordance with Swiss law and generally accepted business practices, our articles of association do not provide quorum requirements generally applicable to general meetings of shareholders. To this extent, our practice varies from the requirement of NASDAQ Listing Rule 5620(c), which requires an issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting stock.

Notice

General meetings of shareholders must be convened by the board of directors at least 20 days before the date of the meeting. The general meeting of shareholders is convened by way of a notice appearing in our official publication medium, currently the Swiss Official Gazette of Commerce. Registered shareholders may also be informed by ordinary mail or e-mail. The notice of a general meeting of shareholders must state the items on the agenda, the proposals to be acted upon and, in case of elections, the names of the nominated candidates. Except in the limited circumstances listed below, a resolution may not be passed at a general meeting without proper notice. This limitation does not apply to proposals to convene an extraordinary general meeting of shareholders or to initiate a special investigation and to appoint a special auditor at the request of a shareholder. No previous notification is required for proposals concerning items included in the agenda or for debates that do not result in a vote.

All of the owners or representatives of our shares may, if no objection is raised, hold a general meeting of shareholders without complying with the formal requirements for convening general meetings of shareholders (a universal meeting). This universal meeting of shareholders may discuss and pass binding resolutions on all matters within the purview of the ordinary general meeting of shareholders, provided that the owners or representatives of all the shares are present at the meeting.

Agenda Requests

Pursuant to Swiss law, one or more shareholders, whose combined shareholdings represent the lower of (i) one tenth of the share capital or (ii) an aggregate nominal value of at least CHF 1,000,000, may request that an

item be included in the agenda for a general meeting of shareholders. To be timely, the shareholder's request must be received by us generally at least 120 calendar days in advance of the meeting. The request must be made in writing and contain, for each of the agenda items, generally the following information:

- a brief description of the business desired to be brought before the ordinary general meeting of shareholders and the reasons for conducting such business at the ordinary general meeting of shareholders;
- the name and address, as they appear in the share register, of the shareholder proposing such business; and
- all other information required under the applicable laws and stock exchange rules.

In addition, if the shareholder intends to solicit proxies from the shareholders of a company, such shareholder shall notify the company of this intent in accordance with Securities and Exchange Commission Rule 14a-4 and/or Rule 14a-8.

Our business report, the compensation report and the auditor's report must be made available for inspection by the shareholders at our registered office no later than 20 days prior to the general meeting of shareholders. Shareholders of record may be notified of this in writing.

Voting Rights

The shareholders exercise their voting rights at the general meetings of shareholders in proportion to the nominal value of the shares belonging to them. The shares are not divisible. The right to vote and the other rights of share ownership may only be exercised by shareholders (including any nominees) or usufructuaries who are entered in our share register at the cut-off date determined by the board of directors. Those entitled to vote in the general meeting of shareholders may be represented by the independent proxy holder (annually elected by the general meeting of shareholders), another registered shareholder or third person with written authorization to act as proxy or the shareholder's legal representative. The chairman has the power to decide whether to recognize a power of attorney.

Our articles contain provisions that prevent investors from acquiring voting rights exceeding 15% of the outstanding share capital. Specifically, no individual or legal entity may, directly or indirectly, control voting rights with respect to 15% or more of the registered share capital recorded in the Commercial Register. In the event that a shareholder should exceed the 15% ownership threshold, the registered shares exceeding the limit of 15% shall be entered in our share registered as shares without voting rights. The board of directors may in special cases approve exceptions to the above regulations.

Furthermore, the board of directors is authorized to withdraw or limit the preemptive rights of the shareholders and to allot them to third parties following a shareholder or a group of shareholders acting in concert having accumulated shareholdings in excess of 15% of the share capital registered in the commercial register without having submitted to the other shareholders a takeover offer recommended by the board of directors, or for the defense of an actual, threatened or potential takeover bid, in relation to which the board of directors, upon consultation with an independent financial adviser retained by it, has not recommended to the shareholders acceptance on the basis that the board of directors has not found the takeover bid to be financially fair to the shareholders.

Our articles contain provisions that persons who do not expressly declare in the registration application that they are holding the shares on their own account (thereafter: nominees) shall forthwith be entered on the share register as shareholders with voting rights up to a maximum of 3% of the share capital. Beyond that limit, registered shares of nominees shall only be entered as voting if the nominees in question confirm in writing that they are willing to disclose the names, addresses and shareholdings of the persons on whose account they hold 0.5% or more of the share capital. The board of directors concludes agreements with nominees that among other things govern the representation of shareholders and the voting rights.

Dividends And Other Distributions

Our board of directors may propose to shareholders that a dividend or other distribution be paid but cannot itself authorize the distribution. Dividend payments require a resolution passed by a simple majority of the shares represented at a general meeting of shareholders regardless of abstentions or empty or invalid votes. In addition, our auditors must confirm that the dividend proposal of our board of directors conforms to Swiss statutory law and our articles of association.

Under Swiss law, we may pay dividends only if we have sufficient distributable profits brought forward from the previous business years *(Gewinnvortrag)*, or if we have distributable reserves *(freie Reserven)*, each as evidenced by our audited stand-alone statutory balance sheet prepared pursuant to Swiss law, and after allocations to reserves required by Swiss law and the articles of association have been deducted. We are not permitted to pay interim dividends out of profit of the current business year.

Distributable reserves are generally booked either as "free reserves" *(freie Reserven)* or as "reserve from capital contributions"*(Kapitaleinlagereserven)*. Under the CO, if our general reserves *(allgemeine Reserven)* amount to less than 20% of our share capital recorded in the commercial register (i.e., 20% of the aggregate nominal value of our issued capital), then at least 5% of our annual profit must be retained as general reserves. The CO permits us to accrue additional general reserves. Further, a purchase of our own shares (whether by us or a subsidiary) reduces the distributable reserves in an amount corresponding to the purchase price of such own shares. Finally, the CO under certain circumstances requires the creation of revaluation reserves which are not distributable.

Distributions out of issued share capital (i.e. the aggregate nominal value of our issued shares) are not allowed and may be made only by way of a share capital reduction. Such a capital reduction requires a resolution passed by a simple majority of the shares represented at a general meeting of shareholders regardless of abstentions or empty or invalid votes. The resolution of the shareholders must be recorded in a public deed and a special audit report must confirm that claims of our creditors remain fully covered despite the reduction in the share capital recorded in the commercial register. The licensed special audit expert must be present at the general meeting of shareholders which adopts such resolution. The share capital may be reduced below CHF 100,000 only if and to the extent that at the same time the statutory minimum share capital of CHF 100,000 is reestablished by sufficient new fully paid-up capital. Upon approval by the general meeting of shareholders of the capital reduction, the board of directors must give public notice of the capital reduction resolution in the Swiss Official Gazette of Commerce three times and notify creditors that they may request, within two months of the third publication, satisfaction of or security for their claims. The reduction of the share capital may be implemented only after expiration of this time limit.

Our board of directors determines the date on which the dividend entitlement starts. Dividends are usually due and payable shortly after the shareholders have passed the resolution approving the payment, but shareholders may also resolve at the ordinary general meeting of shareholders to pay dividends in quarterly or other installments.

For a discussion of the taxation of dividends, see "Taxation—Swiss Tax Considerations—Taxation of Common Shares—Swiss Federal Withholding Tax on Dividends and Distributions."

Transfer Of Shares

Shares in uncertificated form *(Wertrechte)* may only be transferred by way of assignment. Shares that constitute intermediated securities *(Bucheffekten)* may only be transferred when a credit of the relevant intermediated securities to the acquirer's securities account is made in accordance with the relevant provisions of the FISA.

Inspection Of Books And Records

Under the CO, a shareholder has a right to inspect our share register with respect to his own shares and otherwise to the extent necessary to exercise his shareholder rights. No other person has a right to inspect our share register. Our books and correspondence may be inspected with the express authorization of the general meeting of shareholders or by resolution of the board of directors and subject to the safeguarding of our business secrets. See "Comparison of Swiss Law and Delaware Law—Inspection of Books and Records."

Special Investigation

If the shareholders' inspection rights as outlined above prove to be insufficient in the judgment of the shareholder, any shareholder may propose to the general meeting of shareholders that specific facts be examined by a special commissioner in a special investigation. If the general meeting of shareholders approves the proposal, we or any shareholder may, within 30 calendar days after the general meeting of shareholders, request a court sitting in Basel, Switzerland, our registered office, to appoint a special commissioner. If the general meeting of shareholders rejects the request, one or more shareholders representing at least 10 percent of the share capital or holders of shares in an aggregate nominal value of at least CHF 2.0 million may request that the court appoint a special commissioner. The court will issue such an order if the petitioners can demonstrate that the founder members, the board of directors, any member of the board of directors or our executive management infringed the law or our articles of association and thereby caused damages to the Company or the shareholders. The costs of the investigation would generally be allocated to us and only in exceptional cases to the petitioners.

Compulsory Acquisitions; Appraisal Rights

Business combinations and other transactions that are governed by the Swiss Merger Act (i.e. mergers, demergers, transformations and certain asset transfers) are binding on all shareholders. A statutory merger or demerger requires approval of two-thirds of the shares represented at a general meeting of shareholders and the absolute majority of the nominal value of the shares represented.

If a transaction under the Swiss Merger Act receives all of the necessary consents, all shareholders are compelled to participate in such transaction.

Swiss corporations may be acquired by an acquirer through the direct acquisition of the share capital of the Swiss corporation. The Swiss Merger Act provides for the possibility of a so-called "cash-out" or "squeeze-out" merger if the acquirer controls 90% of the outstanding shares. In these limited circumstances, minority shareholders of the corporation being acquired may be compensated in a form other than through shares of the acquiring corporation (for instance, through cash or securities of a parent corporation of the acquiring corporation or of another corporation). For business combinations effected in the form of a statutory merger or demerger and subject to Swiss law, the Swiss Merger Act provides that if equity rights have not been adequately preserved or compensation payments in the transaction are unreasonable, a shareholder may request the competent court to determine a reasonable amount of compensation.

In addition, under Swiss law, the sale of "all or substantially all of our assets" by us may require the approval of two-thirds of the shares represented at a general meeting of shareholders and the absolute majority of the nominal value of the shares represented. Whether a shareholder resolution is required depends on the particular transaction, including whether the following test is satisfied:

- a core part of our business is sold without which it is economically impracticable or unreasonable to continue to operate the remaining business;
- our assets, after the divestment, are not invested in accordance with our statutory business purpose; and
- the proceeds of the divestment are not earmarked for reinvestment in accordance with our business purpose but, instead, are intended for distribution to our shareholders or for financial investments unrelated to our business.

A shareholder of a Swiss corporation participating in certain major corporate transactions may, under certain circumstances, be entitled to appraisal rights. As a result, such shareholder may, in addition to the consideration (be it in shares or in cash) receive an additional amount to ensure that the shareholder receives the fair value of the shares held by the shareholder. Following a statutory merger or demerger, pursuant to the Swiss Merger Act, shareholders can file an appraisal action against the surviving company. If the consideration is deemed inadequate, the court will determine an adequate compensation payment.

Board Of Directors

Our articles of association provide that the board of directors shall consist of at least and not more than members.

The members of the board of directors and the chairman are elected annually by the general meeting of shareholders for a period until the completion of the subsequent ordinary general meeting of shareholders and are eligible for re-election. Each member of the board of directors must be elected individually.

Powers

The board of directors has the following non-delegable and inalienable powers and duties:

- the ultimate direction of the business of the Company and issuing of the relevant directives;
- laying down the organization of the Company;
- formulating accounting procedures, financial controls and financial planning systems as required for the management of the company;
- nominating and removing persons entrusted with the management and representation of the Company and regulating the power to sign for the Company;
- the ultimate supervision of those persons entrusted with management of the Company, with particular regard to adherence to law, our articles of association, and regulations and directives of the Company;
- issuing the annual report and the compensation report, and preparing for the general meeting of shareholders and carrying out its resolutions; and
- informing the court in case of over-indebtedness.

The board of directors may, while retaining such non-delegable and inalienable powers and duties, delegate some of its powers, in particular direct management, to a single or to several of its members, managing directors, committees or to third parties who need be neither members of the board of directors nor shareholders. Pursuant to Swiss law and Article 25 of our articles of association, details of the delegation and other procedural rules such as quorum requirements must be set forth in the organizational rules issued by the board of directors.

Indemnification of Executive Management and Directors

Subject to Swiss law, Article 29 of our articles of association provides for indemnification of the existing and former members of the board of directors, executive management and their heirs, executors and administrators, against liabilities arising in connection with the performance of their duties in such capacity, and permits us to advance the expenses of defending any act, suit or proceeding to our directors and executive management.

In addition, under general principles of Swiss employment law, an employer may be required to indemnify an employee against losses and expenses incurred by such employee in the proper execution of their duties under the

employment agreement with the employer. See "Comparison of Swiss Law and Delaware Law—Indemnification of directors and executive management and limitation of liability."

We have entered or will enter into indemnification agreements with each of the members of our board of directors and executive management. See "Related Party Transactions—Indemnification Agreements."

Conflict Of Interest; Management Transactions

Swiss law does not have a general provision regarding conflicts of interest. However, the CO contains a provision that requires our directors and executive management to safeguard the Company's interests and imposes a duty of loyalty and duty of care on our directors and executive management. This rule is generally understood to disqualify directors and executive management from participation in decisions that directly affect them. Our directors and executive officers are personally liable to us for any breach of these provisions. In addition, Swiss law contains provisions under which directors and all persons engaged in the Company's management are liable to the Company, each shareholder and the Company's creditors for damages caused by an intentional or negligent violation of their duties. Furthermore, under Swiss law, shareholders and members of the board of directors and their close associates who have unduly and in bad faith received dividends, shares of profits paid to board members, other shares of profits or similar are obliged to return such benefits. They are likewise obliged to return other benefits received from the company to the extent these are manifestly disproportionate to the performance rendered in return and to the company's economic situation.

Upon the closing of this offering, our board of directors will adopt a Code of Business Conduct and Ethics that will cover a broad range of matters, including the handling of conflicts of interest.

Principles of the Compensation of the Board Of Directors and the Executive Management

Pursuant to Swiss law, beginning at our first annual meeting as a public company in 2016 our shareholders must annually approve the compensation of the board of directors and the persons whom the board of directors has, fully or partially, entrusted with the management of the Company. The board of directors must issue, on an annual basis, a written compensation report that must be reviewed together with a report on our business by our auditor. The compensation report must disclose all compensation, loans and other forms of indebtedness granted by the Company, directly or indirectly, to current or former members of the board of directors and executive management to the extent related to their former role within the Company or not on customary market terms.

The disclosure concerning compensation, loans and other forms of indebtedness must include the aggregate amount for the board of directors and the executive management, as well as the particular amount for each member of the board of directors and executive officer, specifying the name and function of each person.

Certain forms of compensation are prohibited for members of our board of directors and executive management, such as:

- severance payments provided for either contractually or in the articles of association (compensation due until the termination of a contractual relationship does not qualify as severance payment);
- advance compensation;
- incentive fees for the acquisition or transfer of companies, or parts thereof, by the Company or by companies being, directly or indirectly, controlled by us;
- loans, other forms of indebtedness, pension benefits not based on occupational pension schemes and performance-based compensation not provided for in the articles of association; and
- equity securities and conversion and option rights awards not provided for in the articles of association.

Compensation to members of the board of directors and executive management for activities in entities that are, directly or indirectly, controlled by the Company is prohibited if the compensation (i) would have been prohibited if it was paid directly by the Company, (ii) is not provided for in the articles of association or (iii) has not been approved by the general meeting of shareholders.

Beginning in 2017, the general meeting of shareholders will annually vote on the proposals of the board of directors with respect to:

- the maximum aggregate amount of the non-performance-related compensation of the board of directors for the subsequent term of office;
- the maximum aggregate amount of possible additional compensation of the board of directors for the preceding business year;
- the maximum aggregate amount of non-performance-related compensation of the executive management for the 12-month period starting on 1 July following the general meeting of shareholders;
- the maximum aggregate amount of variable compensation of the executive management for the current year; and
- the maximum grant of options of shares in the company to the board of directors and the executive management.

In the event that, at the general meeting of shareholders, the shareholders do not approve a proposal of the board of directors, the board of directors may form a new proposal for the maximum aggregate compensation and the particular compensation for each individual, taking into account all relevant factors, and submit the new proposal for approval by the same general meeting of shareholders, at a subsequent extraordinary general meeting or determine a maximum total remuneration or several maximum partial remunerations, subject to the relevant principles of the compensation, and submit these to the next general meeting of shareholders.

In addition to fixed compensation, members of the executive management may be paid variable compensation, depending on the achievement of certain performance criteria. The variable compensation depends on the Company's business success and the individual performance of the member of the executive management based on the achievement of the pre-determined targets during a business year. The board of directors determines annually at the beginning of each relevant business year the decisive targets and their weighting upon proposal by the compensation, nomination and corporate governance committee. The amount of the performance-related compensation for each member of the executive management is determined by the board of directors and may not exceed 100 percent of the respective individual fixed remuneration for the same year.

Compensation may be paid or granted in the form of cash, shares, financial instruments, in kind, or in the form of other types of benefits. The board of directors or, where delegated to it, the compensation, nomination and corporate governance committee shall determine grant, vesting, exercise and forfeiture conditions.

Borrowing Powers

The members of the board of directors and the executive management may not be granted any loans, credits or securities. Excepted from the above are advances in the maximum amount of CHF 0.5 million per person for attorneys' fees, court and other similar costs required for the defense of third-party liability claims to the extent permitted by the articles of association of the Company.

Repurchases of Shares and Purchases of Our Own Shares

The CO limits our right to purchase and hold our own shares. We and our subsidiaries may purchase shares only if and to the extent that (i) we have freely distributable reserves in the amount of the purchase price; and

(ii) the aggregate nominal value of all shares held by us does not exceed 10 percent of our share capital. Pursuant to Swiss law, where shares are acquired in connection with a transfer restriction set out in the articles of association, the foregoing upper limit is 20 percent. If we own shares that exceed the threshold of 10 percent of our share capital, the excess must be sold or cancelled by means of a capital reduction within two years.

Shares held by us or our subsidiaries are not entitled to vote at the general meeting of shareholders but are entitled to the economic benefits applicable to the shares generally, including dividends and pre-emptive rights in the case of share capital increases.

In addition, selective share repurchases are only permitted under certain circumstances. Within these limitations, as is customary for Swiss corporations, we may purchase and sell our own shares from time to time in order to meet imbalances of supply and demand, to provide liquidity and to even out variances in the market price of shares.

Notification And Disclosure Of Substantial Share Interests

The disclosure obligations generally applicable to shareholders of Swiss corporations under the Swiss Financial Market Infrastructure Act do not apply to us since our shares are not listed on a Swiss exchange.

Pursuant to art. 663c of the CO, Swiss corporations whose shares are listed on a stock exchange must disclose their significant shareholders and their shareholdings in the notes to their balance sheet, where this information is known or ought to be known. Significant shareholders are defined as shareholders and groups of shareholders linked through voting rights who hold more than five percent of all voting rights.

Stock Exchange Listing

We intend to apply to list our common shares on the NASDAQ Global Market under the symbol “CRSP”.

The Depository Trust Company

Initial settlement of the common shares issued in this offering will take place on the consummation date of this offering through The Depository Trust Company, or DTC, in accordance with its customary settlement procedures for equity securities. Each person owning common shares held through DTC must rely on the procedures thereof and on institutions that have accounts therewith to exercise any rights of a holder of the shares.

Transfer Agent and Registrar of Shares

Our share register will initially be kept by , which acts as transfer agent and registrar. The share register reflects only record owners of our shares. Swiss law does not recognize fractional share interests.

COMPARISON OF SWISS LAW AND DELAWARE LAW

The Swiss laws applicable to Swiss corporations and their shareholders differ from laws applicable to U.S. corporations and their shareholders. The following table summarizes significant differences in shareholder rights between the provisions of the Swiss Code of Obligations *(Schweizerisches Obligationenrecht)* and the Swiss Ordinance against excessive compensation in listed stock corporations applicable to our Company, as implemented by the Company in its Articles of Association, and the Delaware General Corporation Law applicable to companies incorporated in Delaware and their shareholders. Please note that this is only a general summary of certain provisions applicable to companies in Delaware. Certain Delaware companies may be permitted to exclude certain of the provisions summarized below in their charter documents.

DELAWARE CORPORATE LAW	SWISS CORPORATE LAW
Mergers and similar arrangements	
Under the Delaware General Corporation Law, with certain exceptions, a merger, consolidation, sale, lease or transfer of all or substantially all of the assets of a corporation must be approved by the board of directors and a majority of the outstanding shares entitled to vote thereon. A shareholder of a Delaware corporation participating in certain major corporate transactions may, under certain circumstances, be entitled to appraisal rights pursuant to which such shareholder may receive cash in the amount of the fair value of the shares held by such shareholder (as determined by a court) in lieu of the consideration such shareholder would otherwise receive in the transaction. The Delaware General Corporation Law also provides that a parent corporation, by resolution of its board of directors, may merge with any subsidiary, of which it owns at least 90.0% of each class of capital stock without a vote by the shareholders of such subsidiary. Upon any such merger, dissenting shareholders of the subsidiary would have appraisal rights.	Under Swiss law, with certain exceptions, a merger or a demerger of the corporation or a sale of all or substantially all of the assets of a corporation must be approved by two-thirds of the voting rights represented at the respective general meeting of shareholders as well as the absolute majority of the nominal value of shares represented at such shareholders' meeting. A shareholder of a Swiss corporation participating in a statutory merger or demerger pursuant to the Swiss Merger Act (Fusionsgesetz*)* can file a lawsuit against the surviving company. If the consideration is deemed "inadequate," such shareholder may, in addition to the consideration (be it in shares or in cash) receive an additional amount to ensure that such shareholder receives the fair value of the shares held by such shareholder. Swiss law also provides that if the merger agreement provides only for a compensation payment, at least 90.0% of all members in the transferring legal entity, who are entitled to vote, shall approve the merger agreement.
Shareholders' suits	
Class actions and derivative actions generally are available to shareholders of a Delaware corporation for, among other things, breach of fiduciary duty, corporate waste and actions not taken in accordance with applicable law. In such actions, the court has discretion to permit the winning party to recover attorneys' fees incurred in connection with such action.	Class actions and derivative actions as such are not available under Swiss law. Nevertheless, certain actions may have a similar effect. A shareholder is entitled to bring suit against directors for breach of their duties and claim the payment of the company's losses or damages both to the corporation and, subject to certain conditions, to the individual shareholder and creditors. Likewise, an appraisal lawsuit won by a shareholder may indirectly compensate all shareholders. Under Swiss law, the winning party is generally entitled to recover or to partially recover attorneys' fees incurred in connection with such action, *provided, however,* that the court has broad discretion to permit the shareholder whose claim has been dismissed to recover attorneys' fees incurred to the extent he or she acted in good faith.

DELAWARE CORPORATE LAW	SWISS CORPORATE LAW
Shareholder vote on board and management compensation	
Under the Delaware General Corporation Law, the board of directors has the authority to fix the compensation of directors, unless otherwise restricted by the certificate of incorporation or bylaws.	Pursuant to the Swiss Ordinance against excessive compensation in listed stock corporations *(Verordnung gegen übermässige Vergütungen bei börsenkotierten Aktiengesellschaften)*, the general meeting of shareholders has the non-transferable right, amongst others, to vote on the fixed and on the variable compensation of the members of the board of directors, of the executive management and of the advisory boards.
Annual vote on board renewal	
Unless directors are elected by written consent in lieu of an annual meeting, directors are elected in an annual meeting of stockholders on a date and at a time designated by or in the manner provided in the bylaws. Re-election is possible. Classified boards are permitted.	The general meeting of shareholders elects annually (i.e. term of office until the end of the following general meeting of shareholders) the members of the board of directors and the members of the compensation, nomination and corporate governance committee individually for a term of office of one year. Re-election is possible.
Indemnification of directors and executive management and limitation of liability	
The Delaware General Corporation Law provides that a certificate of incorporation may contain a provision eliminating or limiting the personal liability of directors (but not other controlling persons) of the corporation for monetary damages for breach of a fiduciary duty as a director, except no provision in the certificate of incorporation may eliminate or limit the liability of a director for: • any breach of a director's duty of loyalty to the corporation or its shareholders; • acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law; • statutory liability for unlawful payment of dividends or unlawful stock purchase or redemption; or • any transaction from which the director derived an improper personal benefit.	Under Swiss corporate law, an indemnification by the corporation of a director or member of the executive management in relation to potential personal liability is not effective to the extent the director or member of the executive management intentionally or negligently violated his or her corporate duties towards the corporation (certain views advocate that at least a grossly negligent violation is required to exclude the indemnification). Furthermore, the general meeting of shareholders may discharge the directors and members of the executive management from liability from actions taken during the past financial year. Such discharge is effective only, however, for disclosed facts and only as against the company and those shareholders who approved the discharge or who have since acquired their shares in full knowledge of the discharge. Most violations of corporate law are regarded as violations of duties towards the corporation rather than towards the shareholders. In addition, indemnification of other controlling persons is not permitted under Swiss corporate law, including shareholders of the corporation.
A Delaware corporation may indemnify any person who was or is a party or is threatened to be made a party to any proceeding, other than an action by or on behalf of the corporation, because the person is or was a director or officer, against liability incurred in connection with the proceeding if the director or officer acted in good	The articles of association of a Swiss corporation may also set forth that the corporation shall indemnify and hold harmless, to the extent permitted by the law, the directors and executive managers out of assets of the corporation against threatened, pending or completed actions.

DELAWARE CORPORATE LAW	SWISS CORPORATE LAW
faith and in a manner reasonably believed to be in, or not opposed to, the best interests of the corporation; and the director or officer, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. Unless ordered by a court, any foregoing indemnification is subject to a determination that the director or officer has met the applicable standard of conduct: • by a majority vote of the directors who are not parties to the proceeding, even though less than a quorum; • by a committee of directors designated by a majority vote of the eligible directors, even though less than a quorum; • by independent legal counsel in a written opinion if there are no eligible directors, or if the eligible directors so direct; or • by the shareholders. Moreover, a Delaware corporation may not indemnify a director or officer in connection with any proceeding in which the director or officer has been adjudged to be liable to the corporation unless and only to the extent that the court determines that, despite the adjudication of liability but in view of all the circumstances of the case, the director or officer is fairly and reasonably entitled to indemnity for those expenses which the court deems proper.	Also, a corporation may enter into and pay for directors' and officers' liability insurance which may cover negligent acts as well.
Directors' fiduciary duties	
A director of a Delaware corporation has a fiduciary duty to the corporation and its shareholders. This duty has two components: • the duty of care; and • the duty of loyalty. The duty of care requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself or herself of, and disclose to shareholders, all material information reasonably available regarding a significant transaction.	A director of a Swiss corporation has a fiduciary duty to the corporation only. This duty has two components: • the duty of care; and • the duty of loyalty. The duty of care requires that a director act in good faith, with the care that an ordinarily prudent director would exercise under similar circumstances. Under this duty, a director must inform himself of, and disclose, all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. This duty prohibits in principle self-dealing by a

DELAWARE CORPORATE LAW	SWISS CORPORATE LAW
	director and mandates that the best interest of the corporation take precedence over any interest possessed by a director or officer. The members of the board of directors must furthermore afford the shareholders equal treatment in equal circumstances. The burden of proof for a violation of these duties is with the corporation or with the shareholder bringing a suit against the director. The board of directors of a Swiss corporation manages the business of the corporation, unless responsibility for such management has been delegated to the executive management (for example by organizational rules and comparable bylaws). However, there are several non-transferable duties of the board of directors: • the overall management of the corporation and the issuing of all necessary directives; • the determination of the corporation's organization; • the organization of the accounting, financial control and financial planning systems as required for the management of the corporation; • the appointment and dismissal of persons entrusted with managing and representing the corporation; • overall supervision of the persons entrusted with managing the corporation, in particular with regard to compliance with the law, articles of association, operational regulations and directives; • compilation of the annual report, preparation for the general meeting, the compensation report and implementation of its resolutions; and • notification of the court in the event that the company is over-indebted. The members of the board of directors must perform their duties with all due diligence and safeguard the interests of the corporation in good faith. They must afford the shareholders equal treatment in equal circumstances. The burden of proof for a violation of these duties is with the corporation or with the shareholder bringing a suit against the director.
The duty of loyalty requires that a director act in a manner he or she reasonably believes to be in the best interests of the corporation. He or she must not use his or her corporate position for personal gain or advantage. This duty prohibits self-dealing by a director and mandates that the best interest of the corporation and its shareholders take precedence over any interest possessed by a director, officer or controlling shareholder and not shared by the shareholders generally. In general, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Should such evidence be presented concerning a transaction by a director, a director must prove the procedural fairness of the transaction, and that the transaction was of fair value to the corporation.	

DELAWARE CORPORATE LAW	SWISS CORPORATE LAW
Shareholder action by written consent	
A Delaware corporation may, in its certificate of incorporation, eliminate the right of shareholders to act by written consent.	Shareholders of a Swiss corporation may only exercise their voting rights in a general meeting of shareholders and may not act by written consents. The articles of association must allow for (independent) proxies to be present at a general meeting of shareholders. The instruction of such (independent) proxies may occur in writing or electronically.
Shareholder proposals	
A shareholder of a Delaware corporation has the right to put any proposal before the annual meeting of shareholders, provided it complies with the notice provisions in the governing documents. A special meeting may be called by the board of directors or any other person authorized to do so in the governing documents, but shareholders may be precluded from calling special meetings.	At any general meeting of shareholders any shareholder may put proposals to the meeting if the proposal is part of an agenda item. No resolution may be made on proposals relating to the agenda items that were not duly notified. Unless the articles of association provide for a lower threshold or for additional shareholders' rights: • shareholders together representing at least 10% of the share capital may demand that a general meeting of shareholders be called for specific agenda items and specific proposals; and • shareholders together representing shares with a nominal value of at least CHF 1.0 million may demand that an agenda item including a specific proposal be put on the agenda for a regularly scheduled general meeting of shareholders, provided such request is made with appropriate notice. Any shareholder can propose candidates for election as directors without prior written notice provided that the election of board members has been included as an agenda item. In addition, any shareholder is entitled, at a general meeting of shareholders and without advance notice, to (i) request information from the board on the affairs of the company (note, however, that the right to obtain such information is limited), (ii) request information from the auditors on the methods and results of their audit, (iii) request to convene an extraordinary general meeting or (iv) request to carry out a special audit and to appoint a special auditor.
Cumulative voting	
Under the Delaware General Corporation Law, cumulative voting for elections of directors is not permitted unless the corporation's certificate of incorporation provides for it.	Cumulative voting is not permitted under Swiss corporate law. Pursuant to Swiss law, shareholders can vote for each proposed candidate, but they are not allowed to cumulate their votes for single candidates. An annual individual election of (i) all members of the board of directors, (ii) the chairman of the board of

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	directors, (iii) the members of the compensation, nomination and corporate governance committee, (iv) the election of the independent proxy for a term of office of one year (i.e. until the following annual general meeting) as well as the vote on the compensation for the members of the board of directors and the executive management as well as for the members of the advisory board, if applicable, is mandatory for listed companies. Re-election is permitted.
Removal of directors	
A Delaware corporation with a classified board may be removed only for cause with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise.	A Swiss corporation may remove, with or without cause, any director at any time with a resolution passed by a simple majority of the shares represented at a general meeting of shareholders. The articles of association may require the approval by a qualified majority of the shares represented at a meeting for the removal of a director.
Transactions with interested shareholders	
The Delaware General Corporation Law generally prohibits a Delaware corporation from engaging in certain business combinations with an "interested shareholder" for three years following the date that such person becomes an interested shareholder. An interested shareholder generally is a person or group who or which owns or owned 15.0% or more of the corporation's outstanding voting stock within the past three years.	No such rule applies to a Swiss corporation.
Dissolution; Winding up	
Unless the board of directors of a Delaware corporation approves the proposal to dissolve, dissolution must be approved by shareholders holding 100.0% of the total voting power of the corporation. Only if the dissolution is initiated by the board of directors may it be approved by a simple majority of the corporation's outstanding shares. Delaware law allows a Delaware corporation to include in its certificate of incorporation a supermajority voting requirement in connection with dissolutions initiated by the board.	A dissolution of a Swiss corporation requires the approval by two-thirds of the voting rights represented as well as the absolute majority of the nominal value of the share capital represented at a general meeting of shareholders passing a resolution on such dissolution. The articles of association may increase the voting thresholds required for such a resolution.
Variation of rights of shares	
A Delaware corporation may vary the rights of a class of shares with the approval of a majority of the outstanding shares of such class, unless the certificate of incorporation provides otherwise.	The general shareholder meeting of a Swiss corporation may resolve that preference shares be issued or that existing shares be converted into preference shares with a resolution passed by a simple majority of the shares represented at the general meeting of shareholders. Where a company has issued preference shares, further preference shares conferring preferential rights over the existing preference shares may be issued only with the consent of both a special meeting of the adversely affected holders of the existing preference shares and of

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	a general meeting of all shareholders, unless otherwise provided in the articles of association. Shares with preferential voting rights are not regarded a special class for these purposes.
Amendment of governing documents	
A Delaware corporation's governing documents may be amended with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise.	The articles of association of a Swiss corporation may be amended with a resolution passed by a simple majority of the shares represented at such meeting, unless otherwise provided in the articles of association. There are a number of resolutions, such as an amendment of the stated purpose of the corporation, the introduction of authorized and conditional capital and the introduction of shares with preferential voting rights that require the approval by two-thirds of the voting rights represented and an absolute majority of the nominal value of the shares represented at a shareholders' meeting. The articles of association may increase the voting thresholds.
Inspection of books and records	
Shareholders of a Delaware corporation, upon written demand under oath stating the purpose thereof, have the right during the usual hours for business to inspect for any proper purpose, and to obtain copies of list(s) of shareholders and other books and records of the corporation and its subsidiaries, if any, to the extent the books and records of such subsidiaries are available to the corporation.	Shareholders of a Swiss corporation may only inspect books and records if the general meeting of shareholders or the board of directors approved such inspection. The information may be refused where providing it would jeopardize the corporation's trade secrets or other interests warranting protection. A shareholder is only entitled to receive information to the extent required to exercise such shareholders' rights, subject to the interests of the corporation. The right to inspect the share register is limited to the right to inspect that shareholder's own entry in the share register.
Payment of dividends	
The board of directors may approve a dividend without shareholder approval. Subject to any restrictions contained in its certificate of incorporation, the board may declare and pay dividends upon the shares of its capital stock either: • out of its surplus; or • in case there is no such surplus, out of its net profits for the fiscal year in which the dividend is declared and/or the preceding fiscal year. Stockholder approval is required to authorize capital stock in excess of that provided in the charter. Directors may issue authorized shares without stockholder approval.	Dividend payments are subject to the approval of the general meeting of shareholders. The board of directors may propose to shareholders that a dividend shall be paid but cannot itself authorize the distribution. Payments out of the Company's share capital (in other words, the aggregate nominal value of the Company's registered share capital) in the form of dividends are not allowed; however, payments out of share capital may be made by way of a capital reduction only. Dividends may be paid only from the profits brought forward from the previous business years or if the Company has distributable reserves, each as will be presented on the Company's audited annual stand-alone balance sheet. The dividend may be determined only after the allocations to reserves required by the law and the articles of association have been deducted.

DELAWARE CORPORATE LAW	SWISS CORPORATE LAW
Creation and issuance of new shares	
All creation of shares require the board of directors to adopt a resolution or resolutions, pursuant to authority expressly vested in the board of directors by the provisions of the company's certificate of incorporation.	All creation of shares requires a shareholders' resolution. An authorized or contingent capital increase requires at least two-thirds of the voting rights represented at the general meeting of shareholders and an absolute majority of the nominal value of shares represented. Authorized shares can be, once created by shareholder resolution, issued by the board of directors (subject to fulfillment of the authorization). Conditional shares are created and issued through the exercise of options and conversion rights related to debt instruments issued by the board of directors or such rights issued to employees.

COMMON SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there was no public market for our common shares. Future sales of substantial amounts of our common shares in the public market could adversely affect market prices prevailing from time to time. Furthermore, because only a limited number of common shares will be available for sale shortly after this offering due to existing contractual and legal restrictions on resale as described below, there may be sales of substantial amounts of our common shares in the public market after such restrictions lapse. This may adversely affect the prevailing market price and our ability to raise equity capital in the future.

Upon completion of this offering, we will have common shares outstanding assuming no exercise of the underwriters' over-allotment option. Of these shares, common shares, or common shares if the underwriters exercise their over-allotment option in full to purchase additional common shares, sold in this offering will be freely transferable without restriction or registration under the Securities Act, except for any common shares purchased by one of our existing "affiliates," as that term is defined in Rule 144 under the Securities Act. The remaining common shares outstanding are "restricted shares" as defined in Rule 144. Restricted shares may be sold in the public market only if registered or if they qualify for an exemption from registration under Rules 144 or 701 of the Securities Act. After the expiration of the contractual 180-day lock-up period described below, these common shares may be sold in the public market only if registered or pursuant to an exemption under Rules 144 or 701, which are summarized below.

Additionally, of the options to purchase common shares outstanding as of , 2016 and assuming no outstanding options are exercised and no exercise of the underwriters' over-allotment option to purchase additional shares, options exercisable for common shares will be vested and eligible for sale 180 days after the date of this prospectus.

Rule 144

In general, a person who has beneficially owned our common shares that are restricted shares for at least six months would be entitled to sell such securities, provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, the sale and (ii) we are subject to, and in compliance with certain of, the Exchange Act periodic reporting requirements for at least 90 days before the sale. If such person has beneficially owned such common shares for at least one year, then the requirement in clause (ii) will not apply to the sale.

Persons who have beneficially owned our common shares that are restricted shares for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1% of the number of our common shares then outstanding, which will equal approximately common shares immediately after this offering, assuming no exercise of the underwriters' over-allotment option; or
- the average weekly trading volume of our common shares on the NASDAQ during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale;

provided, in each case, that we are subject to, and in compliance with certain of, the Exchange Act periodic reporting requirements for at least 90 days before the sale. Such sales must also comply with the manner of sale and notice provisions of Rule 144.

Affiliate resales under Rule 144 are also subject to the availability of current public information about us. In addition, if the number of shares being sold under Rule 144 by an affiliate during any three-month period exceeds 5,000 shares or has an aggregate sale price in excess of $50,000, the seller must file a notice on Form 144 with the Securities and Exchange Commission and concurrently with either the placing of a sale order with the broker or the execution directly with a market maker.

In general, under Rule 144 as currently in effect, once we have been subject to the public company reporting requirements of Section 13 or Section 15(d) of the Exchange Act for at least 90 days, a person who is not deemed to have been one of our affiliates for purposes of the Securities Act at any time during the 90 days preceding a sale and who has beneficially owned the shares proposed to be sold for at least six months, including the holding period of any prior owner other than our affiliates, is entitled to sell those shares without complying with the manner of sale, volume limitation or notice provisions of Rule 144, subject to compliance with the public information requirements of Rule 144. If such a person has beneficially owned the shares proposed to be sold for at least one year, including the holding period of any prior owner other than our affiliates, then that person would be entitled to sell those shares without complying with any of the requirements of Rule 144.

Rule 701

In general, under Rule 701, any of our employees, directors, officers, consultants or advisors who purchases shares from us in connection with a compensatory share or option plan or other written agreement before the effective date of this offering is entitled to resell such shares 90 days after the effective date of this offering in reliance on Rule 144, without having to comply with the holding period requirements or other restrictions contained in Rule 701.

The SEC has indicated that Rule 701 will apply to typical share options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after the date of this prospectus. Securities issued in reliance on Rule 701 are restricted securities and, subject to the contractual restrictions described below, beginning 90 days after the date of this prospectus, may be sold by persons other than "affiliates," as defined in Rule 144, subject only to the manner of sale provisions of Rule 144 and by "affiliates" under Rule 144 without compliance with the one-year minimum holding period requirement.

Shareholder Registration Rights

Pursuant to the Shareholders' Agreement, after the closing of this offering, certain holders of our common shares, including certain holders of five percent of our capital stock and entities affiliated with certain of our directors, will be entitled to certain rights with respect to registration of such shares under the Securities Act. These shares are referred to as registrable securities. Beginning 180 days after the completion of this offering, the holders of 7,290,487 common shares, including those issuable upon the conversion of shares of our preferred shares upon the closing of this offering, are entitled to the demand, piggyback and Form S-3 registration rights described below.

The registration of registrable securities pursuant to the exercise of the registration rights would enable the holders to trade these registrable securities without restriction under the Securities Act when the applicable registration statement is declared effective. We will pay the registration expenses of the shares registered pursuant to the demand, piggyback and Form S-3 registrations described below.

Generally, in an underwritten offering, the underwriters, if any, have the right, subject to specified conditions, to limit the number of registrable securities the holders may include. The demand, piggyback and Form S-3 registration rights described below will expire five years after the closing of this offering, or with respect to any particular holder, at such time that such holder can sell its shares under Rule 144 of the Securities Act during any ninety (90) day period.

Demand Registration Rights

The holders of the registrable securities will be entitled to certain demand registration rights. At any time beginning 180 days following the effective date of the registration statement, of which this prospectus forms a part, the holders of at least two-thirds ($66^{2/3}\%$) of the registrable securities then outstanding may make a written

request that we register all or a portion of their registrable securities, subject to certain specified exceptions. Such request for registration must cover securities the aggregate proceeds of which, after payment of underwriting discounts, commissions and other expenses related to such registration, would exceed $10,000,000. In no event will we be required to effect more than two (2) demand registrations.

Piggyback Registration Rights

In connection with this offering, the holders of registrable securities were entitled to, and the necessary percentage of holders waived, their rights to notice of this offering and to include their registrable securities in this offering. If we propose to register for offer and sale any of our securities under the Securities Act in another offering, either for our own account or for the account of other security holders, the holders of registrable securities will be entitled to certain "piggyback" registration rights allowing them to include their registrable securities in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act in connection with a public offering for our own account or for the account of any shareholder, the holders of these registrable securities are entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of shares included in the registration, to include their registrable securities in the registration.

Form S-3 Registration Rights

Upon the completion of this offering, the holders of registrable securities will be entitled to certain Form S-3 registration rights. Any holder of registrable securities can make a request that we register for offer and sale all or any portion of their registrable securities on Form S-3 if we are qualified to file a registration statement on Form S-3, subject to certain specified exceptions. Such request for registration on Form S-3 must cover securities the aggregate offering price of which, before payment of the underwriting discounts and commissions, equals or exceeds $2.0 million. We will not be required to effect more than one (1) registration on Form S-3 within any 12-month period.

Options to Purchase Common Shares

We intend to file one or more registration statements on Form S-8 under the Securities Act to register all common shares issued or issuable pursuant to the exercise of outstanding options and reserved for issuance under our new omnibus equity incentive plan. We expect to file the registration statements, which will become effective immediately upon filing, shortly after the date of this prospectus. Shares covered by these registration statements will then be eligible for sale in the public markets, subject to vesting restrictions and any applicable holding periods, any applicable lock-up agreements described below and Rule 144 limitations applicable to affiliates.

Regulation S

Regulation S provides generally that sales made in offshore transactions are not subject to the registration or prospectus-delivery requirements of the Securities Act.

Lock-up Agreements

All of our directors, executive officers and the holders of all of our capital stock have agreed, subject to limited exceptions, not to offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise dispose of, directly or indirectly, or enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common shares or such other securities for a period of 180 days after the date of this prospectus without the prior written consent of Citigroup Global Markets Inc. and Piper Jaffray & Co. See "Underwriting."

TAXATION

The following summary does not purport to address all tax consequences of this offering, the acquisition, the ownership and sale or other disposition of our common shares (such shares for the purposes of this "Taxation" section, "Shares") and does not take into account the specific circumstances of any particular investor. This summary is based on the tax laws, regulations and regulatory practices of Switzerland and the United States as in effect on the date hereof, which are subject to change (or subject to changes in interpretation), possibly with retroactive effect.

Current and prospective shareholders are advised to consult their own tax advisers in light of their particular circumstances as to the Swiss or U.S. tax laws, regulations and regulatory practices that could be relevant for them in connection with this offering, the acquiring, owning and selling or otherwise disposing of Shares and receiving dividends and similar cash or in-kind distributions on Shares (including dividends on liquidation proceeds and stock dividends) or distributions on Shares based upon a capital reduction (Kapitalherabsetzung durch Nennwertreduktion) or reserves paid out of capital contributions (Kapitaleinlagen) and the consequences thereof under the tax laws, regulations and regulatory practices of Switzerland and/or the United States.

Swiss Tax Considerations

Swiss Federal, Cantonal And Communal Individual Income Tax And Corporate Income Tax

Non-Resident Shareholders

Except as discussed in the sections titled "—*Swiss Federal Withholding Taxes*" and "—*Foreign Financial Withholding Taxes*," shareholders who are not resident in Switzerland for tax purposes, and who, during the relevant taxation year, have not engaged in a trade or business carried on through a permanent establishment situated in Switzerland for tax purposes (all such shareholders for purposes of this section, "Non-Resident Shareholders"), will not be subject to any Swiss federal, cantonal and communal income tax on dividends and similar cash or in-kind distributions on Shares (including dividends on liquidation proceeds and stock dividends) (such dividends for the purposes of this, "Dividends"), distributions based upon a capital reduction (*Kapitalherabsetzung durch Nennwertreduktion*) and reserves paid out of capital contributions (*Kapitaleinlagen*) on Shares, or capital gains realized on the sale or other disposition of Shares.

Resident Private Shareholders

Swiss resident individuals who hold their Shares as private assets are required to include Dividends, but not distributions based upon a capital reduction (*Kapitalherabsetzung durch Nennwertreduktion*) and reserves paid out of capital contributions (*Kapitaleinlagen*), in their personal income tax return and are subject to Swiss federal, cantonal and communal income tax on any net taxable income for the relevant taxation period, including the Dividends, but not the distributions based upon a capital reduction (*Kapitalherabsetzung durch Nennwertreduktion*) and reserves paid out of capital contributions (*Kapitaleinlagen*). Capital gains resulting from the sale or other disposition of Shares are generally not subject to Swiss federal, cantonal and communal income tax, and conversely, capital losses are not tax-deductible for Resident Private Shareholders (the shareholders referred to in this paragraph for the purposes of this section, "Resident Private Shareholders"). See "—Domestic Commercial Shareholders" below for a summary of the taxation treatment applicable to Swiss resident individuals, who, for income tax purposes, are classified as "professional securities dealers".

Domestic Commercial Shareholders

Corporate and individual shareholders who are resident in Switzerland for tax purposes, and corporate and individual shareholders who are not resident in Switzerland, and who, in each case, hold their Shares as part of a trade or business carried on in Switzerland, in the case of corporate and individual shareholders not resident in Switzerland, through a permanent establishment situated, for tax purposes, in Switzerland, are required to recognize Dividends, distributions based upon a capital reduction (*Kapitalherabsetzung durch*

Nennwertreduktion) and reserves paid out of capital contributions (*Kapitaleinlagen*) received on Shares and capital gains or losses realized on the sale or other disposition of Shares in their income statement for the relevant taxation period and are subject to Swiss federal, cantonal and communal individual or corporate income tax, as the case may be, on any net taxable earnings for such taxation period. The same taxation treatment also applies to Swiss-resident private individuals who, for income tax purposes, are classified as "professional securities dealers" for reasons of, *inter alia*, frequent dealing, or leveraged investments, in shares and other securities (the shareholders referred to in this paragraph for purposes of this section, "Domestic Commercial Shareholders"). Domestic Commercial Shareholders who are corporate taxpayers may be eligible for dividend relief (*Beteiligungsabzug*) in respect of Dividends and distributions based upon a capital reduction (*Kapitalherabsetzung durch Nennwertreduktion*) and reserves paid out of capital contributions (*Kapitaleinlagen*) if the Shares held by them as part of a Swiss business have an aggregate market value of at least CHF 1 million.

Swiss Cantonal and Communal Private Wealth Tax and Capital Taxes

Non-Resident Shareholders

Non-Resident Shareholders are not subject to Swiss cantonal and communal private wealth tax or capital tax.

Resident Private Shareholders and Domestic Commercial Shareholders

Resident Private Shareholders and Domestic Commercial Shareholders who are individuals are required to report their Shares as part of private wealth or their Swiss business assets, as the case may be, and will be subject to Swiss cantonal and communal private wealth tax on any net taxable wealth (including Shares), in the case of Domestic Commercial Shareholders to the extent the aggregate taxable wealth is allocable to Switzerland. Domestic Commercial Shareholders who are corporate taxpayers are subject to Swiss cantonal and communal capital tax on taxable capital to the extent the aggregate taxable capital is allocable to Switzerland.

Swiss Federal Withholding Tax

Dividends that the Company pays on the Shares are subject to Swiss federal withholding tax *(Verrechnungssteuer)* at a rate of 35% on the gross amount of the Dividend. The Company is required to withhold the Swiss federal withholding tax from the Dividend and remit it to the Swiss Federal Tax Administration. Distributions based upon a capital reduction *(Kapitalherabsetzung durch Nennwertreduktion)* and reserves paid out of capital contributions *(Kapitaleinlagen)* are not subject to Swiss federal withholding tax.

The Swiss federal withholding tax on a Dividend will be refundable in full to a Resident Private Shareholder and to a Domestic Commercial Shareholder to the extent the Shares are allocable to Switzerland, who, in each case, *inter alia*, as a condition to a refund, duly reports the Dividend in his individual income tax return as income or recognizes the Dividend in his income statement as earnings, as applicable.

A Non-Resident Shareholder may be entitled to a partial refund of the Swiss federal withholding tax on a Dividend if the country of his or her residence for tax purposes has entered into a bilateral treaty for the avoidance of double taxation with Switzerland and the conditions of such treaty are met. Such shareholders should be aware that the procedures for claiming treaty benefits (and the time required for obtaining a refund) might differ from country to country.

For example, a shareholder who is a resident of the U.S. for the purposes of the bilateral tax treaty between the U.S. and Switzerland is eligible for a partial refund of the amount of the withholding tax in excess of the 15% treaty rate, provided such shareholder: (i) qualifies for benefits under this treaty and qualifies as beneficial owner of the Dividends; (ii) holds, directly or indirectly, less than 10% of the voting stock of the Company; (iii) does not qualify as a pension scheme or retirement arrangement for the purpose of the bilateral treaty; and (iv) does not conduct business through a permanent establishment or fixed base in Switzerland to which the Shares are attributable. Such an eligible U.S. shareholder may apply for a refund of the amount of the withholding tax in excess of the 15% treaty rate. The applicable refund request form may be filed with the Swiss Federal Tax

Administration following receipt of the Dividend and the relevant deduction certificate, however no later than 31 December of the third year following the calendar year in which the Dividend was payable.

Swiss Federal Stamp Taxes

The Company will be subject to and pay to the Swiss Federal Tax Administration a 1% Swiss federal issuance stamp tax *(Emissionsabgabe)* on the consideration received by it for the issuance of the Shares less certain costs incurred in connection with the issuance.

The issuance of the Shares to the initial shareholders at the offering price is not subject to Swiss federal securities turnover tax *(Umsatzabgabe).*

Any subsequent dealings in the Shares, where a bank or another securities dealer in Switzerland, as defined in the Swiss Federal Stamp Tax Act, acts as an intermediary, or is a party, to the transaction, are, subject to certain exemptions provided for in the Swiss Federal Stamp Tax Act, subject to Swiss securities turnover tax at an aggregate tax rate of 0.15% of the consideration paid for such Shares.

Foreign Final Withholding Tax

Under treaties on final withholding taxes of Switzerland with the United Kingdom and Austria (each, a "Contracting State") a Swiss paying agent, as defined in the treaties, is required to levy a flat-rate final withholding tax *(Abgeltungssteuer)* at rates specified in the treaties on certain capital gains and income items (interest, dividends, other income items, all as defined in the treaties), deriving from assets, including the Shares, held in accounts or deposits with a Swiss paying agent by (i) an individual resident in a Contracting State or, (ii) if certain requirements are met, by a domiciliary company *(Sitzgesellschaft)*, an insurance company in connection with a so-called insurance wrapper (*Versicherungsmantel*) or other individuals if the beneficial owner is an individual resident in a Contracting State. The flat-rate tax withheld substitutes the ordinary income tax on the respective capital gains and income items in the Contracting State where the individual is tax resident. In order to avoid the withholding of the flat-rate tax by the Swiss paying agent, such individuals may opt for a disclosure of the respective capital gains and income items to the tax authorities of the Contracting State where they are tax residents. If Swiss federal withholding tax of 35% has been withheld on Dividends, the Swiss paying agent will—to the extent provided in the applicable bilateral treaty for the avoidance of double taxation between Switzerland and the Contracting State—in its own name and on behalf of the relevant shareholder file with the Swiss tax authorities a request for the partial refund of the Swiss federal withholding tax. The Swiss federal withholding tax, which is not refundable according to the bilateral tax treaty (residual tax), is credited against the flat-rate final withholding tax. Subject to the pending ratification of the amendment protocol of May 27, 2015 to the agreement of October 26, 2004 between the European Community and Switzerland, and the conclusion of a superseding agreement between each of the UK and Austria, terminating the treaties, Swiss paying agents will not have to apply the final withholding tax regimes anymore, as they will have to process the automatic exchange of information from that time for UK and Austrian residents.

Material U.S. Federal Income Tax Considerations to U.S. Holders

The following is a summary of material U.S. federal income tax considerations relating to the acquisition, ownership and disposition of the common shares by a U.S. holder (as defined below). This summary addresses only the U.S. federal income tax considerations for U.S. holders that are initial purchasers of the common shares pursuant to this offering and that will hold such common shares as capital assets (generally, property held for investment) for U.S. federal income tax purposes and does not apply to any shares acquired in the concurrent private placement. This summary does not address all U.S. federal income tax matters that may be relevant to a particular U.S. holder. This summary does not address tax considerations applicable to a holder of common shares that may be subject to special tax rules including, without limitation, the following:

- banks, financial institutions or insurance companies;
- brokers, dealers or traders in securities, currencies, commodities, or notional principal contracts;

- tax-exempt entities or organizations, including an “individual retirement account” or “Roth IRA” as defined in Section 408 or 408A of the Code (as defined below), respectively;
- real estate investment trusts, regulated investment companies or grantor trusts;
- persons that hold the common shares as part of a “hedging,” “integrated” or “conversion” transaction or as a position in a “straddle” for U.S. federal income tax purposes;
- partnerships (including entities classified as partnerships for U.S. federal income tax purposes) or other pass-through entities, or persons that will hold the common shares through such an entity;
- certain former citizens or long term residents of the United States;
- holders that own directly, indirectly, or through attribution 10% or more of the voting power or value of the common shares; and
- holders that have a “functional currency” for U.S. federal income tax purposes other than the U.S. dollar.

Further, this summary does not address the U.S. federal estate, gift, or alternative minimum tax considerations, or any U.S. state, local, or non-U.S. tax considerations of the acquisition, ownership and disposition of the common shares.

This description is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code; existing, proposed and temporary U.S. Treasury Regulations promulgated thereunder, administrative and judicial interpretations thereof; and the income tax treaty between the United States and the Swiss Confederation in each case as in effect and available on the date hereof. All the foregoing is subject to change, which change could apply retroactively, and to differing interpretations, all of which could affect the tax considerations described below. We have not received nor do we expect to seek a ruling from the U.S. Internal Revenue Service, or the IRS, regarding any matter discussed herein. There can be no assurances that the IRS will not take a contrary or different position concerning the tax consequences of the acquisition, ownership and disposition of the common shares or that such a position would not be sustained. Holders should consult their own tax advisers concerning the U.S. federal, state, local and non-U.S. tax consequences of acquiring, owning, and disposing of the common shares in their particular circumstances.

For the purposes of this summary, a “U.S. holder” is a beneficial owner of common shares that is (or is treated as), for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity that is treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of the substantial decisions of such trust or has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a United States person.

If a partnership (or any other entity treated as a partnership for U.S. federal income tax purposes) holds common shares, the U.S. federal income tax consequences relating to an investment in the common shares will depend in part upon the status of the partner and the activities of the partnership. Such a partner or partnership should consult its tax advisor regarding the U.S. federal income tax considerations of acquiring, owning and disposing of the common shares in its particular circumstances.

As indicated below, this discussion is subject to U.S. federal income tax rules applicable to a "passive foreign investment company," or a PFIC. As discussed below under "Passive Foreign Investment Company Considerations," we believe we were a PFIC for the 2015 taxable year and will likely be a PFIC with respect to the 2016 taxable year. In addition, as discussed below under "Controlled Foreign Corporation Considerations," we believe that we were a CFC for the taxable year ended December 31, 2015 and that we were likely a CFC prior to this offering in the current taxable year, and thus will be a CFC for the current taxable year. However the Company's analysis with respect to its CFC status and its PFIC status for the current taxable year is still ongoing. It is possible that we will be a CFC for a taxable year following the year of this offering, and if we are a CFC, this discussion assumes that a "U.S. holder" does not include a holder that is a United States person (within the meaning of the Code) who owns or is considered to own 10% or more of the total combined voting power of all classes of our stock entitled to vote. See "Controlled Foreign Corporation Considerations" for more information.

Persons considering an investment in the common shares should consult their own tax advisors as to the particular tax consequences applicable to them relating to the acquisition, ownership and disposition of the common shares, including the applicability of U.S. federal, state and local tax laws and non-U.S. tax laws.

Distributions

Although we do not currently plan to pay dividends, and subject to the discussion under "Passive Foreign Investment Company Considerations" and "Controlled Foreign Corporation Considerations," below, the gross amount of any distribution (before reduction for any amounts withheld in respect of Swiss withholding tax, if any) actually or constructively received by a U.S. holder with respect to common shares will be taxable to the U.S. holder as a dividend to the extent of the U.S. holder's pro rata share of our current and accumulated earnings and profits as determined under U.S. federal income tax principles. Distributions in excess of earnings and profits will be non-taxable to the U.S. holder to the extent of, and will be applied against and reduce, the U.S. holder's adjusted tax basis in the common shares. Distributions in excess of earnings and profits and such adjusted tax basis will generally be taxable to the U.S. holder as either long-term or short-term capital gain depending upon whether the U.S. holder has held the common shares for more than one year as of the time such distribution is received. However, since we do not calculate our earnings and profits under U.S. federal income tax principles, it is expected that any distribution will be reported as a dividend, even if that distribution would otherwise be treated as a non-taxable return of capital or as capital gain under the rules described above. Non-corporate U.S. holders may qualify for the preferential rates of taxation with respect to dividends on common shares applicable to long-term capital gains (i.e., gains from the sale of capital assets held for more than one year) applicable to qualified dividend income (as discussed below) if we are a "qualified foreign corporation" and certain other requirements (discussed below) are met. A non-United States corporation (other than a corporation that is classified as a PFIC for the taxable year in which the dividend is paid or the preceding taxable year) generally will be considered to be a qualified foreign corporation (a) if it is eligible for the benefits of a comprehensive tax treaty with the United States which the Secretary of Treasury of the United States determines is satisfactory for purposes of this provision and which includes an exchange of information provision, or (b) with respect to any dividend it pays on shares of stock which are readily tradable on an established securities market in the United States. We expect that the common shares will be listed on NASDAQ, which is an established securities market in the United States, and we expect the common shares to be readily tradable on NASDAQ. However, there can be no assurance that the common shares will be considered readily tradable on an established securities market in the United States in later years. The company, which is incorporated under the laws of the Swiss Confederation, believes that it qualifies as a resident of Switzerland for purposes of, and is eligible for the benefits of, The Convention between the United States of America and the Swiss Confederation for the Avoidance of Double Taxation with Respect to Taxes on Income, signed on October 2, 1996, or the U.S.-Swiss Tax Treaty, although there can be no assurance in this regard. Further, the IRS has determined that the U.S.-Swiss Tax Treaty is satisfactory for purposes of the qualified dividend rules and that it includes an exchange-of-information program. Therefore, subject to the discussion under "Passive Foreign Investment Company Considerations" and "Controlled Foreign Corporation Considerations," below, such dividends will generally be "qualified dividend income" in the hands of individual U.S. holders, provided that a holding period requirement (more than 60 days

of ownership, without protection from the risk of loss, during the 121-day period beginning 60 days before the ex-dividend date) and certain other requirements are met. The dividends will not be eligible for the dividends-received deduction generally allowed to corporate U.S. holders.

A U.S. holder generally may claim the amount of any Swiss withholding tax as either a deduction from gross income or a credit against U.S. federal income tax liability. However, the foreign tax credit is subject to numerous complex limitations that must be determined and applied on an individual basis. Generally, the credit cannot exceed the proportionate share of a U.S. holder's U.S. federal income tax liability that such U.S. holder's taxable income bears to such U.S. holder's worldwide taxable income. In applying this limitation, a U.S. holder's various items of income and deduction must be classified, under complex rules, as either "foreign source" or "U.S. source." In addition, this limitation is calculated separately with respect to specific categories of income. The amount of a distribution with respect to the common shares that is treated as a "dividend" may be lower for U.S. federal income tax purposes than it is for Swiss income tax purposes, potentially resulting in a reduced foreign tax credit for the U.S. holder. Each U.S. holder should consult its own tax advisors regarding the foreign tax credit rules.

While we do not currently plan to pay any dividends, the currency of any dividends that we may pay is subject to future determination. If we pay any such dividends in a currency other than U.S. dollars (a "foreign currency"), the amount of a distribution paid to a U.S. holder in a foreign currency will be the U.S. dollar value of the foreign currency calculated by reference to the spot exchange rate on the day the U.S. holder receives the distribution, regardless of whether the foreign currency is converted into U.S. dollars at that time. Any foreign currency gain or loss a U.S. holder realizes on a subsequent conversion of foreign currency into U.S. dollars will be U.S. source ordinary income or loss. If dividends received in a foreign currency are converted into U.S. dollars on the day they are received, a U.S. holder should not be required to recognize foreign currency gain or loss in respect of the dividend.

Sale, Exchange or Other Taxable Disposition of the Common Shares

A U.S. holder will generally recognize gain or loss for U.S. federal income tax purposes upon the sale, exchange or other taxable disposition of common shares in an amount equal to the difference between the U.S. dollar value of the amount realized from such sale or exchange and the U.S. holder's tax basis for those common shares. Subject to the discussion under "Passive Foreign Investment Company Considerations" and "Controlled Foreign Corporation Considerations" below, this gain or loss will generally be a capital gain or loss. The adjusted tax basis in the common shares generally will be equal to the U.S. holder's U.S. dollar purchase price of such common shares. Capital gain from the sale, exchange or other taxable disposition of common shares of a non-corporate U.S. holder is generally eligible for a preferential rate of taxation applicable to capital gains, if the non-corporate U.S. holder's holding period determined at the time of such sale, exchange or other taxable disposition for such common shares exceeds one year (i.e., such gain is long-term taxable gain). The deductibility of capital losses for U.S. federal income tax purposes is subject to limitations under the Code. Any such gain or loss that a U.S. holder recognizes generally will be treated as U.S. source income or loss for foreign tax credit limitation purposes.

Medicare Tax

Certain U.S. holders that are individuals, estates or trusts are subject to a 3.8% tax on all or a portion of their "net investment income," which may include all or a portion of their dividend income and net gains from the disposition of common shares. Each U.S. holder that is an individual, estate or trust is urged to consult its tax advisors regarding the applicability of the Medicare tax to its income and gains in respect of its investment in the common shares.

Controlled Foreign Corporation Considerations

Each "Ten Percent Shareholder" (as defined below) in a non-U.S. corporation that is classified as a "controlled foreign corporation," or a CFC, for United States federal income tax purposes generally is required to

include in income for U.S. federal tax purposes such Ten Percent Shareholder's pro rata share of the CFC's "Subpart F income" and investment of earnings in U.S. property, even if the CFC has made no distributions to its shareholders. Subpart F income generally includes dividends, interest, rents and royalties, gains from the sale of securities and income from certain transactions with related parties. In addition, a Ten Percent Shareholder that realizes gain from the sale or exchange of shares in the CFC may be required to classify a portion of such gain as dividend income rather than capital gain (see discussion above in "—Distributions" regarding the tax treatment of dividend income). A non-U.S. corporation generally will be classified as a CFC for United States federal income tax purposes if Ten Percent Shareholders own, directly or indirectly, more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A "Ten Percent Shareholder" is a United States person (as defined by the Code) who owns or is considered to own 10% or more of the total combined voting power of all classes of stock entitled to vote of such corporation. The determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain.

We believe that we were a CFC for the taxable year ended December 31, 2015 and that we were likely a CFC prior to this offering in the current taxable year, and thus will likely be a CFC for the current taxable year. However the Company's analysis with respect to its CFC status for the current tax year is still ongoing. Additionally, it is possible that, following this offering, a shareholder treated as a U.S. person for U.S. federal income tax purposes will acquire, directly or indirectly, enough shares to be treated as a Ten Percent Shareholder and, together with any other Ten Percent Shareholders, cause the Company to be treated as a CFC for a taxable year following the year of this offering. U.S. holders should consult their own tax advisors with respect to the potential adverse U.S. tax consequences of becoming a Ten Percent Shareholder in a CFC. If we are classified as both a CFC and a PFIC, we generally will not be treated as a PFIC with respect to those U.S. holders that meet the definition of a Ten Percent Shareholder during the period in which we are a CFC.

Passive Foreign Investment Company Considerations

If we are classified as a passive foreign investment company in any taxable year, a U.S. holder would be subject to special rules generally intended to reduce or eliminate any benefits from the deferral of U.S. federal income tax that a U.S. holder could derive from investing in a non-U.S. company that does not distribute all of its earnings on a current basis.

A corporation organized outside the United States generally will be classified as a PFIC for U.S. federal income tax purposes in any taxable year in which, after applying certain look-through rules with respect to the income and assets of its subsidiaries, either: (i) at least 75% of its gross income is "passive income" or (ii) at least 50% of the average quarterly value of its total gross assets (which, assuming we were a non-publicly traded CFC for the year being tested, must be measured by the adjusted tax basis of our assets or, if we were a publicly traded CFC or not a CFC for such year, the total value of our assets may be determined in part by reference to the quarterly market value of our common shares, which may be volatile) is attributable to assets that produce "passive income" or are held for the production of "passive income."

Passive income for this purpose generally includes dividends, interest, royalties, rents, gains from commodities and securities transactions, the excess of gains over losses from the disposition of assets which produce passive income, and includes amounts derived by reason of the temporary investment of funds raised in offerings of the common shares. If a non-U.S. corporation owns directly or indirectly at least 25% by value of the stock of another corporation, the non-U.S. corporation is treated for purposes of the PFIC tests as owning its proportionate share of the assets of the other corporation and as receiving directly its proportionate share of the other corporation's income. If we are classified as a PFIC in any year with respect to which a U.S. holder owns the common shares, we will continue to be treated as a PFIC with respect to such U.S. holder in all succeeding years during which the U.S. holder owns the common shares, regardless of whether we continue to meet the tests described above.

Whether we are a PFIC for any taxable year will depend on the composition of our income and the projected composition and estimated fair market values of our assets (or the adjusted tax basis of our assets if we are a CFC but not a publicly traded corporation for the relevant taxable year as determined under the Code) in each year, and because this is a factual determination made annually after the end of each taxable year, there can be no assurance that we will not be considered a PFIC in any taxable year. Assuming we are not a CFC for the current taxable year, the market value of our assets may be determined in large part by reference to the quarterly market price of our common shares, which is likely to fluctuate after the offering. In addition, the composition of our income and assets will be affected by how, and how quickly, we use the cash proceeds from the global offering in our business.

Based on our belief that we were a CFC for the 2015 taxable year and that we were likely a CFC prior to this offering in the current taxable year (and thus are required to determine our PFIC status under the asset test by reference to the adjusted tax basis of our assets) and on certain estimates of our gross income and gross assets, our intended use of proceeds of this offering, and the nature of our business, we believe we were a PFIC for the 2015 taxable year and will likely be a PFIC with respect to the 2016 taxable year. However, the Company's analysis with respect to its PFIC status for the current tax year is still ongoing. Because the total value of our assets may be measured in part by the market value of our common shares in 2017, we expect that we are unlikely to be classified as a PFIC for the taxable year ending December 31, 2017. However, as previously mentioned, we cannot provide any assurances regarding our PFIC status for the past, current or future taxable years.

If we are a PFIC, and you are a U.S. holder, then unless you make one of the elections described below, a special tax regime will apply to both (a) any "excess distribution" by us to you (generally, your ratable portion of distributions in any year which are greater than 125% of the average annual distribution received by you in the shorter of the three preceding years or your holding period for the common shares) and (b) any gain realized on the sale or other disposition, including a pledge, of the common shares. Under this regime, any excess distribution and realized gain will be treated as ordinary income and will be subject to tax as if (a) the excess distribution or gain had been realized ratably over your holding period, (b) the amount deemed realized in each year had been subject to tax in each year of that holding period at the highest marginal rate for such year (other than income allocated to the current period or any taxable period before we became a PFIC, which would be subject to tax at the U.S. holder's regular ordinary income rate for the current year and would not be subject to the interest charge discussed below), and (c) the interest charge generally applicable to underpayments of tax had been imposed on the taxes deemed to have been payable in those years. In addition, dividend distributions made to you will not qualify for the lower rates of taxation applicable to long-term capital gains discussed above under "Distributions."

Certain elections exist that may alleviate some of the adverse consequences of PFIC status and would result in an alternative treatment (such as mark-to-market treatment) of the common shares. If a U.S. holder makes the mark-to-market election, the U.S. holder generally will recognize as ordinary income any excess of the fair market value of the common shares at the end of each taxable year over their adjusted tax basis, and will recognize an ordinary loss in respect of any excess of the adjusted tax basis of the common shares over their fair market value at the end of the taxable year (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). If a U.S. holder makes the election, the U.S. holder's tax basis in the common shares will be adjusted to reflect these income or loss amounts. Any gain recognized on the sale or other disposition of common shares in a year when we are a PFIC will be treated as ordinary income and any loss will be treated as an ordinary loss (but only to the extent of the net amount of income previously included as a result of the mark-to-market election). The mark-to-market election is available only if we are a PFIC and the common shares are "regularly traded" on a "qualified exchange." The common shares will be treated as "regularly traded" in any calendar year in which more than a de minimis quantity of the common shares are traded on a qualified exchange on at least 15 days during each calendar quarter (subject to the rule that trades that have as one of their principal purposes the meeting of the trading requirement as disregarded). NASDAQ is a qualified exchange for this purpose and, consequently, if the common shares are regularly traded, the mark-to-market election will be available to a U.S. holder.

If we are a PFIC for any year during which a U.S. holder holds the common shares, we must generally continue to be treated as a PFIC by that U.S. holder for all succeeding years during which the U.S. holder holds the common shares, unless we cease to meet the requirements for PFIC status and the U.S. holder makes a "deemed sale" election with respect to the common shares. If such election is made, the U.S. holder will be deemed to have sold the common shares it holds at their fair market value on the last day of the last taxable year in which we qualified as a PFIC, and any gain from such deemed sale would be subject to the consequences described above. After the deemed sale election, the U.S. holder's common shares with respect to which the deemed sale election was made will not be treated as shares in a PFIC unless we subsequently become a PFIC.

The tax consequences that would apply if we were a PFIC would also be different from those described above if a U.S. holder were able to make a valid "qualified electing fund," or QEF, election. However, we do not currently intend to provide the information necessary for U.S. holders to make a QEF election if we were treated as a PFIC for any taxable year and prospective investors should assume that a QEF election will not be available. U.S. Holders should consult their tax advisors to determine whether any of the above elections would be available and if so, what the consequences of the alternative treatments would be in their particular circumstances.

If we are determined to be a PFIC, a U.S. holder will generally be treated as owning a proportionate amount (by value) of shares owned by us in any direct or indirect subsidiaries that are also PFICs and will be subject to similar adverse rules with respect to any distributions we receive from, or dispositions we make of, the shares such subsidiaries. The mark-to-market election is not permitted for the shares of any of our subsidiaries that are also classified as PFICs. U.S. holders are urged to consult their tax advisors about the application of the PFIC rules to any of our subsidiaries.

If a U.S. holder owns common shares during any taxable year in which we are a PFIC, the U.S. holder generally will be required to file an IRS Form 8621 (Information Return by a Shareholder of a Passive Foreign Investment Company or Qualified Electing Fund) with respect to the company, generally with the U.S. holder's federal income tax return for that year. If our company were a PFIC for a given taxable year, then you should consult your tax advisor concerning your annual filing requirements.

The U.S. federal income tax rules relating to PFICs are complex. Prospective U.S. investors are urged to consult their own tax advisers with respect to the acquisition, ownership and disposition of the common shares, the consequences to them of an investment in a PFIC, any elections available with respect to the common shares and the IRS information reporting obligations with respect to the acquisition, ownership and disposition of the common shares.

Backup Withholding and Information Reporting

U.S. holders generally will be subject to information reporting requirements with respect to dividends on the common shares and on the proceeds from the sale, exchange or disposition of common shares that are paid within the United States or through U.S.-related financial intermediaries (and certain subsidiaries thereof), unless the U.S. holder is an "exempt recipient." In addition, U.S. holders may be subject to backup withholding on such payments, unless the U.S. holder provides a taxpayer identification number and a duly executed IRS Form W-9 or otherwise establishes an exemption. Backup withholding is not an additional tax, and the amount of any backup withholding will be allowed as a credit against a U.S. holder's U.S. federal income tax liability and may entitle such holder to a refund, provided that the required information is timely furnished to the IRS.

Foreign Asset Reporting

Certain U.S. holders who are individuals are required to report information relating to an interest in the common shares, subject to certain exceptions (including an exception for shares held in accounts maintained by U.S. financial institutions) by filing IRS Form 8938 (Statement of Specified Foreign Financial Assets) with their

federal income tax return. U.S. holders are urged to consult their tax advisors regarding their information reporting obligations, if any, with respect to their ownership and disposition of the common shares.

THE DISCUSSION ABOVE IS A GENERAL SUMMARY. IT DOES NOT COVER ALL TAX MATTERS THAT MAY BE OF IMPORTANCE TO A PARTICULAR PROSPECTIVE INVESTOR. EACH PROSPECTIVE INVESTOR IS URGED TO CONSULT ITS OWN TAX ADVISOR ABOUT THE TAX CONSEQUENCES TO IT OF AN INVESTMENT IN THE SHARES IN LIGHT OF THE INVESTOR'S OWN CIRCUMSTANCES.

UNDERWRITING

Citigroup Global Markets Inc., Piper Jaffray & Co. and Barclays Capital Inc. are acting as joint book-running managers of the offering and as representatives of the underwriters named below. Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus, each underwriter named below has severally agreed to purchase, and we have agreed to sell to that underwriter, the number of shares set forth opposite the underwriter's name.

Underwriter	Number of Shares
Citigroup Global Markets Inc.	
Piper Jaffray & Co.	
Barclays Capital Inc.	
Guggenheim Securities, LLC	
Total	

The underwriting agreement provides that the obligations of the underwriters to purchase the shares included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all the shares (other than those covered by the over-allotment option described below) if they purchase any of the shares.

Shares sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus. Any shares sold by the underwriters to securities dealers may be sold at a discount from the initial public offering price not to exceed $ per share. If all the shares are not sold at the initial public offering price, the underwriters may change the offering price and the other selling terms. The representatives have advised us that the underwriters do not intend to make sales to discretionary accounts.

If the underwriters sell more shares than the total number set forth in the table above, we have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to additional shares at the initial public offering price less the underwriting discount. The underwriters may exercise the option solely for the purpose of covering over-allotments, if any, in connection with this offering. To the extent the option is exercised, each underwriter must purchase a number of additional shares approximately proportionate to that underwriter's initial purchase commitment. Any shares issued or sold under the option will be issued and sold on the same terms and conditions as the other shares that are the subject of this offering.

We, our officers and directors and substantially all of our shareholders have agreed that, subject to specified limited exceptions, for a period ending 180 days following the date of this prospectus, we and they will not, without the prior written consent of Citigroup and Piper Jaffray, dispose of or hedge any shares or any securities convertible into or exchangeable for our common shares. Citigroup and Piper Jaffray in their sole discretion may release any of the securities subject to these lock-up agreements at any time, which, in the case of officers and directors, shall be with notice.

The restrictions described in the immediately preceding paragraph do not apply to our directors, executive officers or shareholders with respect to:

- transfers or dispositions (1) as a bona fide gift, (2) to an immediate family member of the undersigned or to a trust formed for the direct or indirect benefit of the undersigned or an immediate family member of the undersigned, (3) by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or trustee of the undersigned or (4) pursuant to a divorce settlement agreement or decree or a qualified domestic relations order; provided that in each case, each recipient agrees to be bound in writing by the same restrictions, such transfers shall not involve a disposition for

value and no filing under Section 13 or Section 16(a) of the Exchange Act or other public announcement shall be required or voluntarily made during the restricted period;

- transactions relating to common shares acquired in the offering or in open market transactions after the completion of the offering, provided that with respect to such open market transactions, no filing under Section 13 or Section 16(a) of the Exchange Act or other public announcement shall be required or voluntarily made during the restricted period;
- exercise of options or warrants to purchase common shares or the receipt of common shares upon the vesting of restricted common share awards and any related transfer of common shares to us in connection therewith (x) deemed to occur upon the "cashless" or "net" exercise of such options or warrants or (y) for the purpose of paying the exercise price of such options or warrants or for paying taxes due as a result of the exercise of such options or warrants, the vesting of such options, warrants or common share awards, or as a result of the vesting of such common shares, provided that all common shares received upon such exercise, vesting or transfer remain subject to the restrictions on transfer described herein and provided that no filing under Section 13 or Section 16(a) of the Exchange Act or other public announcement shall be required or voluntarily made during the restricted period;
- transfers of common shares to us pursuant to agreements under which we have the option to repurchase such common shares, provided that no filing under Section 13 or Section 16(a) of the Exchange Act or other public announcement shall be required or voluntarily made during the restricted period;
- transfers of common shares to any affiliate (as defined in Rule 405 of the Securities Act of 1933, as amended), limited partners, general partners, limited liability company members or shareholders of the undersigned, or if the undersigned is a corporation to any wholly owned subsidiary of such corporation, provided that in each case, the recipient agrees to be bound in writing by the same restrictions, such transfers shall not involve a disposition for value and no filing under Section 13 or Section 16(a) of the Exchange Act or other public announcement shall be required or voluntarily made during the restricted period;
- the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of common shares, provided that such plan does not provide for the transfer of common shares during the restricted period and no filing under Section 13 or Section 16(a) of the Exchange Act or other public announcement shall be required or voluntarily made during the restricted period; or
- transfers, sales, tenders or other dispositions of common shares pursuant to a bona-fide third-party tender offer, merger, amalgamation, consolidation or other similar transaction made to or involving all holders of the common shares pursuant to a change of control of the ownership of us, provided that such transaction is approved by our board of directors, and if such transaction is not completed, any common shares subject to restrictions described above remain subject to the restrictions for the restricted period.

In addition, the restrictions described above do not apply to us with respect to:

- the common shares to be sold by us in this offering;
- the issuance and sale by us of common shares pursuant to any employee stock option plan, stock ownership plan or dividend reinvestment plan in effect on the date of this offering; and
- the issuance by us of common shares issuable upon the conversion of securities or the exercise of warrants outstanding on the date of this offering.

This lock-up provision applies to common shares and to securities convertible into, or exercisable or exchangeable for such common shares.

Prior to this offering, there has been no public market for our shares. Consequently, the initial public offering price for the shares will be determined by negotiations between us and the representatives. Among the

factors considered in determining the initial public offering price will be our results of operations, our current financial condition, our future prospects, our markets, the economic conditions in and future prospects for the industry in which we compete, our management, and currently prevailing general conditions in the equity securities markets, including current market valuations of publicly traded companies considered comparable to our company. We cannot assure you, however, that the price at which the shares will sell in the public market after this offering will not be lower than the initial public offering price or that an active trading market in our shares will develop and continue after this offering.

We intend to apply to have our shares listed on the Nasdaq Global Market under the symbol "CRSP."

The following table shows the underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters' over-allotment option.

		Total	
	Per Share	No Exercise	Full Exercise
Public offering price	$	$	$
Underwriting discounts and commissions to be paid by us	$	$	$
Proceeds to us, before expenses	$	$	$

We estimate that our portion of the total expenses of this offering, exclusive of underwriting discounts and commissions, will be $. We have agreed to reimburse the underwriters for expenses, in an amount up to $, relating to the clearance of this offering with the Financial Industry Regulatory Authority, Inc and the qualification of our common shares under state securities laws.

In connection with the offering, the underwriters may purchase and sell shares in the open market. Purchases and sales in the open market may include short sales, purchases to cover short positions, which may include purchases pursuant to the underwriters' over-allotment option, and stabilizing purchases.

- Short sales involve secondary market sales by the underwriters of a greater number of shares than they are required to purchase in the offering.
  - "Covered" short sales are sales of shares in an amount up to the number of shares represented by the underwriters' over-allotment option.
  - "Naked" short sales are sales of shares in an amount in excess of the number of shares represented by the underwriters' over-allotment option.
- Covering transactions involve purchases of shares either pursuant to the underwriters' over-allotment option or in the open market in order to cover short positions.
  - To close a naked short position, the underwriters must purchase shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.
  - To close a covered short position, the underwriters must purchase shares in the open market or must exercise their over-allotment option. In determining the source of shares to close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through their over-allotment option.
- Stabilizing transactions involve bids to purchase shares so long as the stabilizing bids do not exceed a specified maximum.

Purchases to cover short positions and stabilizing purchases, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the shares. They may also cause the price of the shares to be higher than the price that would otherwise exist in the open market in the absence of these transactions. The underwriters may conduct these transactions on the Nasdaq Global Market, in the over-the-counter market or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

Conflicts of Interest

The underwriters are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. The underwriters and their respective affiliates may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans and/or credit default swaps) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of shares described in this prospectus may not be made to the public in that relevant member state other than:

- to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- to fewer than 100 or, if the relevant member state has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the relevant Dealer or Dealers nominated by us for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For purposes of this provision, the expression an “offer of securities to the public” in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe for the shares, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, and the expression “Prospectus Directive” means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the relevant member state) and includes any relevant implementing measure in the relevant member state. The expression “2010 PD Amending Directive” means Directive 2010/73/EU.

The sellers of the shares have not authorized and do not authorize the making of any offer of shares through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the shares as contemplated in this prospectus. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of the shares on behalf of the sellers or the underwriters.

Notice to Prospective Investors in the United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the "Order") or (ii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a "relevant person"). This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Notice to Prospective Investors in Australia

No prospectus or other disclosure document (as defined in the Corporations Act 2001 (Cth) of Australia, or Corporations Act) in relation to the shares has been or will be lodged with the Australian Securities & Investments Commission, or ASIC. This document has not been lodged with ASIC and is only directed to certain categories of exempt persons. Accordingly, if you receive this document in Australia:

- you confirm and warrant that you are either:
  - a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
  - a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to us which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
  - a person associated with the company under section 708(12) of the Corporations Act; or
  - a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act, and to the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this document is void and incapable of acceptance; and
- you warrant and agree that you will not offer any of the shares for resale in Australia within 12 months of those shares being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

Notice to Prospective Investors in France

Neither this prospectus nor any other offering material relating to the shares described in this prospectus has been submitted to the clearance procedures of the *Autorité des Marchés Financiers* or of the competent authority of another member state of the European Economic Area and notified to the *Autorité des Marchés Financiers.* The shares have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus nor any other offering material relating to the shares has been or will be:

- released, issued, distributed or caused to be released, issued or distributed to the public in France; or
- used in connection with any offer for subscription or sale of the shares to the public in France.

Such offers, sales and distributions will be made in France only:

- to qualified investors (*investisseurs qualifiés*) and/or to a restricted circle of investors (*cercle restreint d'investisseurs*), in each case investing for their own account, all as defined in, and in accordance with articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French *Code monétaire et financier*;
- to investment services providers authorized to engage in portfolio management on behalf of third parties; or
- in a transaction that, in accordance with article L.411-2-II-1°-or-2°-or 3° of the French *Code monétaire et financier* and article 211-2 of the General Regulations (*Règlement Général*) of the *Autorité des Marchés Financiers*, does not constitute a public offer (*appel public à l'épargne*).

The shares may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French *Code monétaire et financier*.

Notice to Prospective Investors in Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong) and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Notice to Prospective Investors in Japan

The shares offered in this prospectus have not been and will not be registered under the Financial Instruments and Exchange Law of Japan. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, in Japan or to or for the account of any resident of Japan (including any corporation or other entity organized under the laws of Japan), except (i) pursuant to an exemption from the registration requirements of the Financial Instruments and Exchange Law and (ii) in compliance with any other applicable requirements of Japanese law.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to compliance with conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

- to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than $200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;
- where no consideration is or will be given for the transfer; or
- where the transfer is by operation of law.

Notice to Prospective Investors in Canada

The securities may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

CONCURRENT PRIVATE PLACEMENT

Pursuant to a Subscription Agreement dated December 19, 2015, or the Subscription Agreement, Bayer Global Investments B.V., or Bayer BV, has agreed to purchase from us concurrently with this offering in a private placement up to $35 million of our common shares at a price per share equal to the initial public offering price, subject to the terms and conditions set forth in the Subscription Agreement. We may reduce the amount of Bayer BV's purchase in our sole discretion, subject to the terms of the Subscription Agreement. The sale of these shares will not be registered under the Securities Act and the concurrent private placement is subject to certain closing conditions. The shares issued to Bayer BV in the concurrent private placement will be subject to the registration rights contained in the Shareholders' Agreement described in the section entitled "Common Shares Eligible for Future Sale—Shareholder Registration Rights."

The Subscription Agreement provides that, until the later to occur of (i) 18 month anniversary of the closing of this offering or (ii) the termination of the JV Agreement, and subject to certain exceptions, Bayer BV is prohibited from taking certain actions with respect to our capital stock and business operations, including but not limited to:

(a) acquiring, directly or indirectly, any of our equity securities if the acquisition would increase Bayer BV's beneficial ownership percentage in CRISPR by more than 5%, compared to its ownership interest immediately following the closing of this offering;

(b) proposing (i) any merger, consolidation, business combination, tender or exchange offer, sale of all or substantially all of our assets or businesses, or similar transactions involving CRISPR or (ii) any recapitalization, restructuring, liquidation or other extraordinary transaction with respect to CRISPR; or

(c) (i) proposing or seeking, whether alone or in concert with others, any solicitation of proxies or consents to vote any securities of the Company, (ii) nominating any person as a director of our board of directors, (iii) proposing any matter to be voted upon by our shareholders or (iv) acting, alone or in concert with others, to seek to control our management, board of directors, policies or affairs.

Bayer BV has entered into a 180-day lock-up agreement in favor of the underwriters in this offering, including with respect to the shares it purchases in the concurrent private placement. See "Underwriting" for a summary of the terms of the lock-up agreement entered into by Bayer BV, and our directors, officers and substantially all of our shareholders.

LEGAL MATTERS

The validity of the common shares and certain other matters of Swiss law will be passed upon for us by Vischer AG, Zurich, Switzerland. Certain matters of U.S. federal and Delaware state law will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts, and for the underwriters by Ropes & Gray LLP, Boston, Massachusetts.

EXPERTS

The consolidated financial statements of CRISPR Therapeutics AG at December 31, 2015 and 2014 and for the years then ended appearing in the Prospectus and Registration Statement, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

ENFORCEMENT OF JUDGMENTS

We are organized under the laws of Switzerland and our registered office and domicile is located in Basel, Switzerland. Moreover, certain of our directors and executive officers are not residents of the United States, and all or a substantial portion of the assets of such persons are located outside the United States. As a result, it may not be possible for investors to effect service of process within the United States upon us or upon such persons or to enforce against them judgments obtained in U.S. courts, including judgments in actions predicated upon the civil liability provisions of the federal securities laws of the United States. We have been advised by our Swiss counsel that there is doubt as to the enforceability in Switzerland of original actions, or in actions for enforcement of judgments of U.S. courts, of civil liabilities to the extent solely predicated upon the federal and state securities laws of the United States. Original actions against persons in Switzerland based solely upon the U.S. federal or state securities laws are governed, among other things, by the principles set forth in the Swiss Federal Act on Private International Law. This statute provides that the application of provisions of non-Swiss law by the courts in Switzerland shall be precluded if the result would be incompatible with Swiss public policy. Also, mandatory provisions of Swiss law may be applicable regardless of any other law that would otherwise apply.

Switzerland and the United States do not have a treaty providing for reciprocal recognition of and enforcement of judgments in civil and commercial matters. The recognition and enforcement of a judgment of the courts of the United States in Switzerland is governed by the principles set forth in the Swiss Federal Act on Private International Law. This statute provides in principle that a judgment rendered by a non-Swiss court may be enforced in Switzerland only if:

- the non-Swiss court had jurisdiction pursuant to the Swiss Federal Act on Private International Law;
- the judgment of such non-Swiss court has become final and non-appealable;
- the judgment does not contravene Swiss public policy;
- the court procedures and the service of documents leading to the judgment were in accordance with the due process of law; and
- no proceeding involving the same position and the same subject matter was first brought in Switzerland, or adjudicated in Switzerland, or was earlier adjudicated in a third state and this decision is recognizable in Switzerland.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the U.S. Securities and Exchange Commission, the SEC, a registration statement (including amendments and exhibits to the registration statement) on Form S-1 under the Securities Act. This prospectus, which is part of the registration statement, does not contain all of the information set forth in the registration statement and the exhibits and schedules to the registration statement. For further information, we refer you to the registration statement and the exhibits and schedules filed as part of the registration statement. If a document has been filed as an exhibit to the registration statement, we refer you to the copy of the document that has been filed. Each statement in this prospectus relating to a document filed as an exhibit is qualified in all respects by the filed exhibit.

You may review a copy of the registration statement, including exhibits and any schedule filed therewith, and obtain copies of such materials at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330. In addition, the SEC maintains an Internet website that contains reports and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov.

Upon completion of this offering, we will become subject to the informational requirements of the Exchange Act. Accordingly, we will be required to file reports and other information with the SEC, including annual reports on Form 10-K and reports on Form 10-Q. Those reports may be inspected without charge at the locations described above.

CRISPR Therapeutics AG

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Shareholders
CRISPR Therapeutics AG

We have audited the accompanying consolidated balance sheets of CRISPR Therapeutics AG (the "Company") as of December 31, 2015 and 2014, and the related consolidated statements of operations and comprehensive loss, redeemable convertible preferred shares and shareholders' (deficit) equity, and cash flows for the years then ended. These financial statements are the responsibility of the Company's Board of Directors and management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of CRISPR Therapeutics AG at December 31, 2015 and 2014, and the consolidated results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts
May 13, 2016

CRISPR Therapeutics AG
Consolidated Balance Sheets
(In thousands, except share and per share data)

	December 31, 2014	December 31, 2015 Actual	December 31, 2015 Pro Forma (Unaudited)
Assets			
Current assets:			
Cash	$ 945	$155,961	$ 155,961
Accounts receivable	—	339	339
Prepaid expenses and other current assets	23	540	540
Total current assets	968	156,840	156,840
Property and equipment, net	—	1,328	1,328
Intangible assets, net	509	454	454
Restricted cash	50	700	700
Other non-current assets	—	101	101
Total assets	$ 1,527	$159,423	$ 159,423
Liabilities, redeemable convertible preferred shares and shareholders' (deficit) equity			
Current liabilities:			
Accounts payable	$ 211	$ 1,584	$ 1,584
Accrued expenses	1,924	8,430	8,430
Accrued tax liabilities	11	81	81
Other current liabilities	—	60	60
Total current liabilities	2,146	10,155	10,155
Convertible loan, including accrued interest of $0 and $97 as of December 31, 2014 and 2015, respectively, and $0 pro forma	—	38,336	—
Deferred revenue	—	75,090	75,090
Other non-current liabilities	85	445	445
Total liabilities	2,231	124,026	85,690
Commitments and contingencies (Note 8)	—	—	—
Redeemable convertible preferred shares:			
Series A-1 redeemable convertible preferred shares, CHF 0.10 par value, 132,000 shares authorized, issued, and outstanding in share capital at December 31, 2014 and 2015, no shares issued and outstanding in share capital pro forma (unaudited); aggregate liquidation preference of CHF 502 ($501) at December 31, 2015, and none pro forma (unaudited)	1,169	1,169	—
Series A-2 redeemable convertible preferred shares, CHF 0.10 par value, 936,000 shares authorized, issued, and outstanding in share capital at December 31, 2014 and 2015, no shares issued and outstanding in share capital pro forma (unaudited); aggregate liquidation preference of CHF 9,512 ($9,496) at December 31, 2015, and none pro forma (unaudited)	5,101	10,394	—
Series A-3 redeemable convertible preferred shares, CHF 0.10 par value, 0 and 3,227,401 shares authorized, issued, and outstanding in share capital at December 31, 2014 and 2015, respectively, no shares issued and outstanding in share capital pro forma (unaudited); aggregate liquidation preference of $22,850 at December 31, 2015, and none pro forma (unaudited)	—	22,518	—
Series B redeemable convertible preferred shares, CHF 0.10 par value, 0 and 1,355,704 shares authorized, issued, and outstanding in share capital at December 31, 2014 and 2015, respectively, no shares issued and outstanding in share capital pro forma (unaudited); aggregate liquidation preference of CHF 28,000 ($27,952) at December 31, 2015, and none pro forma (unaudited)	—	30,440	—
Shareholders' (deficit) equity:			
Common shares, CHF 0.10 par value, 1,068,000 and 1,698,642 shares authorized and issued 1,068,000 and 1,658,428 outstanding in share capital at December 31, 2014 and 2015, respectively; 8,641,234 shares issued and outstanding in share capital pro forma (unaudited); 0, 733,309 and 634,904 shares in conditional capital at December 31, 2014, 2015, and pro forma (unaudited), respectively	120	181	879
Additional paid-in capital	1,168	4,636	106,972
Accumulated deficit	(8,403)	(33,906)	(34,110)
Accumulated other comprehensive loss	(2)	(8)	(8)
Total CRISPR Therapeutics AG shareholders' (deficit) equity	(7,117)	(29,097)	73,733
Noncontrolling interest	143	(27)	—
Total shareholders' (deficit) equity	(6,974)	(29,124)	73,733
Total liabilities, redeemable convertible preferred shares and shareholders' (deficit) equity	$ 1,527	$159,423	$ 159,423

See accompanying notes to these consolidated financial statements.

CRISPR Therapeutics AG
Consolidated Statement of Operations and Comprehensive Loss
(In thousands, except share and per share data)

	Year Ended December 31,	
	2014	2015
Collaboration revenue	$ —	$ 247
Operating expenses:		
Research and development	1,513	12,573
General and administrative	5,114	13,403
Total operating expenses	6,627	25,976
Loss from operations	(6,627)	(25,729)
Other (expense) income:		
Interest expense	—	(108)
Other (expense) income, net	(236)	16
Total other expense, net	(236)	(92)
Net loss before benefit from (provision for) income taxes	(6,863)	(25,821)
Benefit from (provision for) income taxes	63	(7)
Net loss	(6,800)	(25,828)
Foreign currency translation adjustment	(2)	(6)
Comprehensive loss	$ (6,802)	$ (25,834)
Reconciliation of net loss to net loss attributable to common shareholders:		
Net loss	$ (6,800)	$ (25,828)
Loss attributable to noncontrolling interest	536	325
Loss on extinguishment of redeemable convertible preferred shares	(745)	—
Net loss attributable to common shareholders	$ (7,009)	$ (25,503)
Net loss per share attributable to common shareholders—basic and diluted	$ (6.56)	$ (16.88)
Weighted-average common shares outstanding used in net loss per share attributable to common shareholders—basic and diluted	1,068,000	1,511,225
Pro forma net loss per share attributable to common shareholders—basic and diluted (unaudited)		$ (4.20)
Pro forma weighted-average common shares used in net loss per share attributable to common shareholders—basic and diluted (unaudited)		6,072,412

See accompanying notes to these consolidated financial statements.

CRISPR Therapeutics AG
Consolidated Statements of Redeemable Convertible Preferred Shares and Shareholders' (Deficit) Equity
(In thousands, except share and per share data)

	Series A-1 Redeemable Convertible Preferred Shares		Series A-2 Redeemable Convertible Preferred Shares		Series A-3 Redeemable Convertible Preferred Shares		Series B Redeemable Convertible Preferred Shares		Common Shares		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total CRISPR Therapeutics AG Shareholders' (Deficit) Equity	Noncontrolling Interest	Total Shareholders' (Deficit) Equity
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	CHF 0.10 Par Value						
Balance at December 31, 2013	132,000	$ 424	—	$ —	—	$ —	—	$ —	1,068,000	$ 98	$ 1,460	$ (2,139)	$ —	$ (581)	$ —	$ (581)
Receipt of common shares subscription receivable	—	—	—	—	—	—	—	—	—	22	—	—	—	22	—	22
Issuance of Series A-2 preferred shares, net of issuance costs of $36 and subscription receivable of $5,293	—	—	936,000	5,101	—	—	—	—	—	—	—	—	—	—	—	—
Loss on extinguishment of Series A-1 preferred shares	—	745	—		—	—	—	—	—	—	(745)	—	—	(745)	—	(745)
Other comprehensive income (loss)	—	—	—	—	—	—	—	—	—	—	—	—	(2)	(2)	—	(2)
Equity-based compensation expense	—	—	—	—	—	—	—	—	—	—	453	—	—	453	242	695
Noncontrolling interest upon consolidation of TRACR Hematology Limited	—	—	—	—	—	—	—	—	—	—	—	—	—	—	437	437
Net loss	—	—	—	—	—	—	—	—	—	—	—	(6,264)	—	(6,264)	(536)	(6,800)
Balance at December 31, 2014	132,000	$ 1,169	936,000	$ 5,101	—	$ —	—	$ —	1,068,000	$ 120	$ 1,168	$ (8,403)	$ (2)	$ (7,117)	$ 143	$ (6,974)
Receipt of Series A-2 preferred shares subscription receivable	—	—	—	5,293	—	—	—	—	—	—	—	—	—	—	—	—
Issuance of Series A-3 preferred shares, net of issuance costs of $332 and subscription receivable of $22,850	—	—	—	—	3,227,401	22,518	—	—	—	—	—	—	—	—	—	—
Adjustment to noncontrolling interest upon share exchange transaction for TRACR Hematology Limited	—	—	—	—	—	—	—	—	590,428	61	1	—	—	62	(62)	—
Issuance of Series B preferred shares, net of issuance costs of $38	—	—	—	—	—	—	1,355,704	30,440	—	—	—	—	—	—	—	—
Equity-based compensation expense	—	—	—	—	—	—	—	—	—	—	3,467	—	—	3,467	217	3,684
Other comprehensive income (loss)	—	—	—	—	—	—	—	—	—	—	—	—	(6)	(6)	—	(6)
Net loss	—	—	—	—	—	—	—	—	—	—	—	(25,503)	—	(25,503)	(325)	(25,828)
Balance at December 31, 2015	132,000	$ 1,169	936,000	$ 10,394	3,227,401	$ 22,518	1,355,704	$ 30,440	1,658,428	$ 181	$ 4,636	$ (33,906)	$ (8)	$ (29,097)	$ (27)	$ (29,124)
Conversion of convertible loan into Series B preferred shares (unaudited)	—	—	—	—	—	—	1,233,296	38,336	—	—	—	—	—	—	—	—
Conversion of redeemable convertible preferred shares into common shares (unaudited)	(132,000)	(1,169)	(936,000)	(10,394)	(3,227,401)	(22,518)	(2,589,000)	(68,776)	6,884,401	688	102,169	—	—	102,857	—	102,857
Exercise of call option for noncontrolling interest (unaudited)	—	–	—	—	—	—	—	—	98,405	10	167	(204)	—	(27)	27	—
Pro forma Balance at December 31, 2015 (unaudited)	—	$ —	—	$ —	—	$ —	—	$ —	8,641,234	$ 879	$ 106,972	$ (34,110)	$ (8)	$ 73,733	$ —	$ 73,733

See accompanying notes to these consolidated financial statements.

CRISPR Therapeutics AG
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31, 2014	2015
Operating activities		
Net loss	$ (6,800)	$ (25,828)
Reconciliation of net loss to net cash used in operating activities:		
Depreciation and amortization expense	38	127
Equity-based compensation expense	695	3,684
Non-cash interest expense	—	97
Unrealized foreign currency remeasurement loss	(260)	(20)
Changes in:		
Restricted cash	(16)	(650)
Prepaid expenses and other assets	(12)	(959)
Accounts payable and accrued expenses	1,583	7,708
Deferred revenue	—	75,090
Deferred rent	—	165
Other liabilities, net	(21)	14
Net cash (used in) provided by operating activities	(4,793)	59,428
Investing activities		
Purchase of property and equipment	—	(1,154)
Net cash used in investing activities	—	(1,154)
Financing activities		
Proceeds from issuance of convertible loan	—	38,239
Proceeds from issuance of common shares	22	—
Proceeds from issuance of restricted shares	—	243
Proceeds from issuance of Series A-2 preferred shares	5,137	5,293
Proceeds from issuance of Series A-3 preferred shares	—	22,850
Proceeds from issuance of Series B preferred shares	—	30,478
Issuance costs for preferred share financings	(36)	(370)
Net cash provided by financing activities	5,123	96,733
Effect of exchange rate changes on cash	254	9
Increase in cash	584	155,016
Cash, beginning of period	361	945
Cash, end of period	$ 945	$ 155,961
Supplemental disclosure of non-cash investing and financing activities		
Property and equipment purchases in accounts payable and accrued expenses	$ —	$ 246
Loss on extinguishment of Series A-1 preferred shares	$ 745	$ —
Non controlling interest upon consolidation of TRACR	$ 547	$ —

See accompanying notes to these consolidated financial statements.

CRISPR Therapeutics AG
Notes to Consolidated Financial Statements

1. Organization and Operations

The Company

CRISPR Therapeutics AG ("CRISPR" or the "Company") was formed on October 28, 2013 in Basel, Switzerland. The Company was established to translate CRISPR/Cas9, a genome editing technology, into transformative gene-based medicines for the treatment of serious human diseases. The foundational intellectual property underlying the Company's operations was licensed to the Company and its subsidiaries in April 2014. The Company devotes substantially all of its efforts to product research and development activities, initial market development and raising capital. The Company's principal offices and operations are in Cambridge, Massachusetts.

On January 23, 2014, the founders of the Company formed TRACR Hematology Limited ("TRACR") in the United Kingdom, to further the development of the CRISPR/Cas9 technology into medicines for the treatment of blood-borne illnesses. As the Company was funding and managing TRACR's operations in 2014, it has been consolidated by the Company from the date that the Company established a variable interest in TRACR in April 2014. In April 2015, the Company acquired 82.1% of the outstanding equity of TRACR in a share exchange transaction.

On February 7, 2014, the Company formed a wholly-owned subsidiary in the United Kingdom, CRISPR Therapeutics Limited ("CRISPR Ltd."), and on February 16, 2015, the Company formed a wholly-owned subsidiary in the United States, CRISPR Therapeutics, Inc. ("CRISPR Inc."), as its principal research and development operation.

The Company is subject to risks common to companies in the biotechnology industry, including but not limited to, risks of failure of preclinical studies and clinical trials, the need to obtain marketing approval for any drug product candidate that it may identify and develop, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations and ability to transition from pilot-scale manufacturing to large-scale production of products.

The Company had an accumulated deficit of $33.9 million as of December 31, 2015 and has financed its operations to date from proceeds obtained from a series of preferred shares and convertible loan issuances and upfront fees received under its collaboration arrangement. The Company will require substantial additional capital to fund its research and development and ongoing operating expenses.

Liquidity

The Company believes its cash of $156.0 million at December 31, 2015 will be sufficient to fund the Company's current operating plan for at least the next 12 months. Thereafter, the Company will be required to obtain additional funding. The Company intends to pursue a public offering of its common shares ("Common Shares") to fund future operations. If the Company is unable to complete a sufficient public offering in a timely manner, it would need to pursue other financing alternatives, such as private financing of debt or equity or collaboration agreements. There can be no assurances, however, that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all.

2. Summary of Significant Accounting Policies

Basis of Presentation and Use of Estimates

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"), and include the accounts of (i) the

Company, (ii) its wholly-owned subsidiaries, CRISPR Ltd. and CRISPR Inc., and (iii) TRACR, a consolidated variable interest entity ("VIE") as of December 31, 2014 and an 82.1% owned subsidiary as of December 31, 2015. All intercompany accounts and transactions have been eliminated. Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASUs") of the Financial Accounting Standards Board ("FASB").

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, equity-based compensation expense, revenue recognition, and reported amounts of expenses during the reported period. Significant estimates in these consolidated financial statements have been made in connection with the calculation of revenues, research and development expenses, equity-based compensation expense, fair value of Common Shares, fair value of intangible assets, and the provision for or benefit from income taxes. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

The Company utilizes significant estimates and assumptions in determining the fair value of its Common Shares. The Company utilized various valuation methodologies in accordance with the framework of the 2004 and 2013 American Institute of Certified Public Accountants Technical Practice Aids, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of its Common Shares. Each valuation methodology includes estimates and assumptions that require the Company's judgment. These estimates and assumptions include a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector, the prices at which the Company sold preferred shares, the superior rights and preferences of securities senior to the Company's Common Shares at the time, the likelihood of achieving a liquidity event, such as an initial public offering or a sale of the Company, and the Company's discounted cash flows from forecasted operations. Significant changes to the key assumptions used in the valuations could result in different fair values of Common Shares at each valuation date and materially affect the financial statements.

Unaudited Pro Forma Information

On May 13, 2016, the Company's Board of Directors authorized the Company to file a registration statement with the Securities and Exchange Commission ("SEC") permitting the Company to sell Common Shares to the public. Upon the closing of a qualified (as defined in the Company's Articles of Incorporation) initial public offering ("IPO"), all of the Company's convertible loan plus accrued interest will convert into redeemable convertible preferred shares and the outstanding redeemable convertible preferred shares will automatically convert into Common Shares. In addition, upon the closing of the IPO, the remaining 17.9% of the ordinary share capital of TRACR, representing the noncontrolling interest, will automatically convert into 98,405 Common Shares. The accompanying unaudited pro forma balance sheet and statement of redeemable convertible preferred shares and shareholders' (deficit) equity as of December 31, 2015 reflect the assumed conversion of the convertible loan and accrued interest into Series B Redeemable Convertible Preferred Shares ("Series B Preferred Shares") and all of the outstanding Series A-1 Redeemable Convertible Preferred Shares ("Series A-1 Preferred Shares"), the Series A-2 Redeemable Convertible Preferred Shares ("Series A-2 Preferred Shares"), the Series A-3 Redeemable Convertible Preferred Shares ("Series A-3 Preferred Shares"), the Series B Preferred Shares (collectively "Preferred Shares") and the remaining noncontrolling interest into Common Shares. See Note 10 for further discussion of the Preferred Shares conversion features, as well as the rights and preferences of the Preferred Shares.

Unaudited pro forma net loss per share attributable to common shareholders is computed using the weighted-average number of Common Shares outstanding after giving effect to the conversion of all Preferred Shares into Common Shares as if such conversion had occurred at the beginning of the period presented, or the

date of original issuance, if later. As the years ended December 31, 2014 and December 31, 2015, resulted in net losses, there is no income allocation required under the two-class method or dilution attributed to pro forma weighted-average shares outstanding in the calculation of pro forma diluted loss per share attributable to common shareholders.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company and the Company's chief operating decision maker, namely, the chief executive officer, view the Company's operations and manage its business in one operating segment, which is the business of discovering, developing and commercializing therapies derived from or incorporating genome-editing technology.

Foreign Currency Translation and Transactions

The Company's reporting currency is the U.S. Dollar. The Company's consolidated entities have the U.S. dollar as their functional currency with the exception of CRISPR Ltd. which has the British Pound Sterling ("GBP") as its functional currency. CRISPR Ltd. has assets and liabilities translated into U.S. dollars at exchange rates in effect at the end of the year. Revenue and expenses are translated using the average exchange rates for the period. Net unrealized gains and losses resulting from foreign currency translation are included in accumulated other comprehensive income (loss), which is a separate component of shareholders' (deficit) equity. Net foreign currency exchange transaction gains and losses resulting from the remeasurement of transactions denominated in currencies other than functional currency are included in other (expense) income, net in the consolidated statements of operations and comprehensive loss.

Cash and Cash Equivalents

The Company considers all highly liquid investments with maturities of 90 days or less from the purchase date to be cash equivalents. As of December 31, 2014 and 2015, the Company had no cash equivalents. All cash was held in depository accounts and is reported at fair value.

Accounts Receivable

There were no accounts receivables at December 31, 2014. Accounts receivable of $0.3 million at December 31, 2015 consist of receivables from Vertex Pharmaceuticals, Incorporated ("Vertex") and are recorded at invoiced amounts due under the Vertex collaboration agreement (see Note 9). As Vertex is a creditworthy entity and maintains an ongoing relationship with the Company, the Company did not have an allowance for estimated losses recorded related to these receivable.

Concentrations of Credit Risk and Off-balance Sheet Risk

Financial instruments that potentially subject the Company to concentrations of credit risk are primarily cash. The Company's cash is held in accounts with financial institutions that management believes are creditworthy. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. The Company has no financial instruments with off-balance sheet risk of loss.

Deferred Public Offering Costs

Deferred public offering costs, which primarily consist of direct, incremental legal and accounting fees relating to the IPO, are capitalized within other assets. The deferred issuance costs will be offset against IPO

proceeds upon the consummation of the offering. In the event the offering is terminated, deferred offering costs will be expensed. The Company had incurred $0.1 million in IPO costs as of December 31, 2015.

Fair Value of Financial Instruments

The Company's financial instruments consist of accounts payable, accrued expenses and other non-current liabilities. The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. FASB ASC Topic 820, *Fair Value Measurement and Disclosures* ("ASC 820"), established a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available. Observable inputs are inputs that market participants would use in pricing the financial instrument based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the financial instrument and are developed based on the best information available in the circumstances.

The accounting standard describes a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value, which are the following:

Level 1	—	Quoted prices in active markets that are accessible at the market date for identical unrestricted assets or liabilities.
Level 2	—	Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs for which all significant inputs are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
Level 3	—	Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amount of accounts receivable, accounts payable, accrued expenses, and convertible loan as reported on the consolidated balance sheets as of December 31, 2014 and 2015, approximate fair value, due to the short-term duration of these instruments. The Company may elect to measure financial instruments and certain other items at fair value at specified election dates in the future.

Property and Equipment

Property and equipment is stated at cost, less accumulated depreciation. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred. Upon disposal, the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss is included in the results of operations. Depreciation is recorded using the straight-line method over the estimated useful lives of the respective assets, which are as follows:

Asset	Estimated useful life
Computer equipment and software	3 years
Furniture, fixtures, and other	5 years
Laboratory equipment	5 years
Leasehold Improvements	Shorter of useful life or remaining lease term

Impairment of Long-lived Assets

The Company evaluates long-lived assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book value of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book value of the assets exceed their fair value. The Company has not recognized any impairment losses in the years ended December 31, 2014 and 2015.

Revenue Recognition

To date, the Company's only source of revenue has been the collaboration and license agreement with Vertex (see Note 9).

The Company recognizes revenue in accordance with ASC Topic 605, *Revenue Recognition* ("ASC 605"). Accordingly, revenue is recognized for each unit of accounting when all of the following criteria are met:

- Persuasive evidence of an arrangement exists;
- Delivery has occurred or services have been rendered;
- The seller's price to the buyer is fixed or determinable; and
- Collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified in current liabilities. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue within non-current liabilities.

The Company evaluates multiple-element arrangements based on the guidance in FASB ASC Topic 605-25, *Revenue Recognition—Multiple-Element Arrangements* ("ASC 605-25"). Pursuant to the guidance in ASC 605-25, the Company evaluates multiple-element arrangements to determine (i) the deliverables included in the arrangement and (ii) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. When deliverables are separable, consideration received is allocated to the separate units of accounting based on the relative selling price method and the appropriate revenue recognition principles are applied to each unit. When the Company determines that an arrangement should be accounted for as a single unit of accounting, the Company must determine the period over which the performance obligations will be performed and revenue will be recognized. This evaluation requires the Company to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that (i) the delivered item has value to the collaboration partner on a standalone basis and (ii) if the arrangement includes a general right of return with respect to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the Company's control. In assessing whether an item has standalone value, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can use any other deliverable for its intended purpose without the receipt of the remaining deliverable, whether the value of the deliverable is dependent on the undelivered item, and whether there are other vendors that can provide the undelivered items.

The consideration received under the arrangement that is fixed or determinable is then allocated among the separate units of accounting based on the relative selling prices of the separate units of accounting. The Company determines the selling price of a unit of accounting within each arrangement following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, the Company determines the estimated selling price for units of

accounting within each arrangement using vendor-specific objective evidence ("VSOE") of selling price, if available; third-party evidence ("TPE") of selling price if VSOE is not available; or best estimate of selling price ("BESP") if neither VSOE nor TPE is available. The Company typically uses BESP to estimate the selling price as it generally does not have VSOE or TPE of selling price for its units of accounting. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company periodically validates the BESP used for units of accounting by evaluating whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

The Company recognizes arrangement consideration allocated to each unit of accounting when all of the following criteria are met for that particular unit of accounting: persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the seller's price to the buyer is fixed or determinable, and collectability is reasonably assured. In the event that a deliverable does not represent a separate unit of accounting, the Company recognizes revenue from the combined unit of accounting over the contractual or estimated performance period for the undelivered items, which is typically the term of the Company's research and development obligations. If there is no discernible pattern of performance or objectively measurable performance measures do not exist, then the Company recognizes revenue under the arrangement on a straight-line basis over the period the Company is expected to complete its performance obligations. Conversely, if the pattern of performance over which the service is provided to the customer can be determined and objectively measurable performance measures exist, then the Company recognizes revenue under the arrangement using the proportional performance method. Revenue recognized is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method or proportional performance method, as applicable, as of the period ending date.

Significant management judgment is required in determining the level of effort required under an arrangement and the period over which the Company expects to complete its performance obligations under an arrangement. Steering committee services that are not inconsequential or perfunctory and that are determined to be performance obligations are combined with other research services or performance obligations required under an arrangement, if any, in determining the level of effort required in an arrangement and the period over which the Company expects to complete its aggregate performance obligations.

At the inception of an arrangement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (i) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item as a result of a specific outcome resulting from the Company's performance to achieve the milestone, (ii) the consideration relates solely to past performance, and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone and the level of effort and investment required to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. The Company will recognize revenue in its entirety upon successful accomplishment of any substantive milestones, assuming all other revenue recognition criteria are met. Milestones that are not considered substantive are recognized as earned if there are no remaining performance obligations or over the remaining period of performance, with a cumulative catch-up being recognized for the elapsed portion of the period of performance, assuming all other revenue recognition criteria are met.

The Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

Research and Development Expenses

Research and development costs, which include employee compensation costs, facilities, lab supplies and materials, overhead, preclinical development, and other related costs, are charged to expense as incurred. Research and development costs also include the costs the Company incurs in its performance of services or provision of materials in connection with the funded research undertaken as a part of the Company's collaborative agreement with Vertex. See Note 9 for further details.

Operating Leases

The Company leases office and laboratory facilities under a non-cancelable operating lease agreements. The lease agreements contain free or escalating rent payment provisions. The Company recognizes rent expense under such leases on a straight-line basis over the term of the lease with the difference between the expense and the payments recorded as deferred rent on the consolidated balance sheets. Lease renewal periods are considered on a lease-by-lease basis in determining the lease term.

Equity-based Compensation Expense

The Company recognizes equity-based compensation expense for awards of equity instruments to employees and non-employee directors (including awards granted by Fay Participation Corp., See Note 12) based on the grant date fair value of those awards in accordance with FASB ASC Topic 718, *Stock Compensation* ("ASC 718"). ASC 718 requires all equity-based compensation awards to employees and non-employee directors, including grants of restricted shares and stock options, to be recognized as expense in the statements of operations based on their grant date fair values. The Company estimates the fair value of stock options using the Black-Scholes option pricing model. The Company uses the value of its Common Shares to determine the fair value of restricted share awards.

The Company accounts for stock options issued to non-employees under FASB ASC Topic 505-50, *Equity-Based Payments to Non-Employees* ("ASC 505-50"). As such, the value of such options is periodically remeasured and income or expense is recognized over their vesting terms. Compensation cost related to awards with service-based vesting schedules is recognized using the straight-line method.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (i) the expected share price volatility, (ii) the calculation of expected term of the award, (iii) the risk-free interest rate and (iv) the expected dividend yield. Due to the lack of a public market for the trading of the Company's Common Shares and a lack of company-specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The group of representative companies have characteristics similar to the Company, including stage of product development and focus on the life science industry. The Company uses the simplified method, which is the average of the final vesting tranche date and the contractual term, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. For options granted to non-employees, the Company utilizes the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The Company uses an assumed dividend yield of zero as the Company has never paid dividends and has no current plans to pay any dividends on its Common Shares.

The Company expenses the fair value of its equity-based compensation awards granted to employees on a straight-line basis over the associated service period, which is generally the period in which the related services are received. The Company measures equity-based compensation awards granted to non-employees at fair value as the awards vest and recognizes the resulting value as compensation expense at each financial reporting period.

The Company records the expense for equity-based compensation awards subject to performance-based milestone vesting over the remaining service period when management determines that achievement of the milestone is probable. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date. There have only been three such awards to date.

Patent Costs

Costs to secure and prosecute patent application and other legal costs related to the protection of the Company's intellectual property are expensed as incurred, and are classified as general and administrative expenses in the Company's consolidated statements of operations.

Income Taxes

Income taxes are recorded in accordance with FASB ASC Topic 740, *Income Taxes* ("ASC 740"), which provides for deferred taxes using an asset and liability approach. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial reporting and tax reporting basis of assets and liabilities and are measured using enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company has evaluated available evidence and concluded that the Company may not realize all the benefit of its deferred tax assets; therefore a valuation allowance has been established for the amount of the deferred tax assets that the Company does not believe is more likely than not to be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2014 and 2015, the Company does not have any significant uncertain tax positions. The Company's practice is to recognize interest and/or penalties related to income tax matters in income tax expense. See Note 13 for further details.

Comprehensive Loss

Comprehensive loss consists of net income or loss and changes in equity during the period from transactions and other events and circumstances generated from non-owner sources. The Company's net loss equals comprehensive loss, net of any changes in the foreign currency translation adjustment, for all periods presented. In addition, comprehensive loss attributable to the noncontrolling interest equals net loss for all periods presented.

Variable Interest Entities

The Company reviews each legal entity formed by parties related to the Company to determine whether or not the Company has a variable interest in the entity and whether or not the entity would meet the definition of a VIE in accordance with FASB ASC Topic 810, *Consolidation* ("ASC 810"). If the entity is a VIE, the Company assesses whether or not the Company is the primary beneficiary of that VIE based on a number of factors, including (i) which party has the power to direct the activities that most significantly affect the VIE's economic performance, (ii) the parties' contractual rights and responsibilities pursuant to any contractual agreements and (iii) which party has the obligation to absorb losses or the right to receive benefits from the VIE. If the Company determines it is the primary beneficiary of a VIE, the Company consolidates the financial statements of the VIE into the Company's consolidated financial statements at the time that determination is made. The Company evaluates whether it continues to be the primary beneficiary of any consolidated VIEs on a quarterly basis. If the Company were to determine that it is no longer the primary beneficiary of a consolidated VIE, or no longer has a variable interest in the VIE, it would deconsolidate the VIE in the period that the determination is made.

If the Company determines it is the primary beneficiary of a VIE that meets the definition of a business, the Company measures the assets, liabilities and noncontrolling interests of the newly consolidated entity at fair value in accordance with FASB ASC Topic 805, *Business Combinations* ("ASC 805") at the date the reporting entity first becomes the primary beneficiary.

For the years ended December 31, 2014 and 2015, the Company consolidated the financial statements of TRACR into the Company's consolidated financial statements as a VIE. See Note 4 for further details.

Noncontrolling Interest

The Company records noncontrolling interest, which relates to TRACR, a consolidated VIE as of December 31, 2014 and a majority owned subsidiary as of December 31, 2015, on its consolidated balance sheets. The Company records net loss (income) attributable to noncontrolling interest on its consolidated statements of operations, reflecting the loss (income) from noncontrolling interest for the reporting period, which is evaluated each reporting period. See Note 4 for further details related to TRACR.

Intangible Assets

The Company's intangible assets consist of acquired intellectual property rights and relate to the Company's interest in TRACR. Intangible assets are recorded at fair value at the date of the business combination and are stated in the consolidated balance sheets net of accumulated amortization and impairments, if applicable. The Company evaluates the remaining useful life of intangible assets subject to amortization on a periodic basis to determine whether events and circumstances would indicate impairment or warrant a revision to the remaining useful life. If the estimate of an intangible asset's remaining useful life is changed, the Company amortizes the remaining carrying value of the intangible asset prospectively over the revised remaining useful life.

Intangible assets related to the acquired intellectual property rights are amortized over their estimated useful lives using the straight-line method as the pattern of revenues cannot be reasonably estimated. Amortization related to the acquired intellectual property rights is recorded in general and administrative expense in the consolidated statements of operations and comprehensive loss. See Note 4 for further details relating to the noncontrolling interest related to TRACR.

Net Loss Per Share Attributable to Common Shareholders

Basic net loss per Common Share is calculated by dividing the net loss attributable to common shareholders by the weighted-average number of Common Shares outstanding during the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common shareholders by the weighted-average number of Common Shares and potentially dilutive securities outstanding for the period determined using the treasury-stock and if-converted methods.

For purposes of the diluted net loss per share calculation, redeemable convertible preferred shares, convertible notes and unvested restricted Common Shares are considered to be potentially dilutive securities, but are excluded from the calculation of diluted net loss per share because their effect would be antidilutive and therefore, basic and diluted net loss per share were the same for all periods presented.

Subsequent Events

The Company considers events or transactions that occur after the balance sheet date but prior to the date the financial statements are available to be issued for potential recognition or disclosure in the financial statements. The Company has completed an evaluation of all subsequent events after the audited balance sheet date of December 31, 2015 through May 13, 2016 the date the financial statements are available to be issued, to ensure that this filing includes appropriate disclosure of events recognized in the financial statements as of December 31, 2015, and events which occurred subsequently but were not recognized in the financial statements. See Note 16 for further details concerning events subsequent to the balance sheet date.

Recent Accounting Pronouncements

In May 2014, the FASB issued ASU 2014-9, *Revenue from Contacts with Customers* ("ASU 2014-09"), updated guidance and disclosure requirements for recognizing revenue. The new revenue recognition standard provides a five-step analysis of transactions to determine when and how revenue is recognized. The revenue standard is based on the principle that revenue should be recognized to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. In March 2016, the FASB issued an amendment to the standard, ASU 2016-8, *Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations (Reporting Revenue Gross versus Net)* ("ASU 2016-08"), which clarifies the implementation guidance on principal versus agent considerations. In April 2016, the FASB issued an additional amendment to the standard, ASU 2016-10, *Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing* ("ASU 2016-10"), which clarifies the guidance on identifying performance obligations and the implementation guidance on licensing. The collective guidance will be effective for the Company on January 1, 2018, with early adoption permitted, but not earlier than January 1, 2017. The guidance may be applied retrospectively to each prior period presented or retrospectively with the cumulative effect recognized as of the date of initial adoption. The Company is currently assessing the potential impact of the adoption of these standards on its consolidated financial statements.

In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements—Going Concern* (Subtopic 205-40): Disclosure of Uncertainties about an Entity's ability to Continue as a Going Concern ("ASU 2014-15"), which requires management to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. This guidance is effective for the annual reporting period ending after December 15, 2016 and for annual and interim periods thereafter. Early adoption is permitted. The Company expects the new guidance will only effect the disclosures in its consolidated financial statements.

In November 2014, the FASB issued ASU No. 2014-16, *Derivatives and Hedging* (Topic 815)—*Determining Whether the Host Contract in a Hybrid Financial Instrument Issued in the Form of a Share is More Akin to Debt or to Equity* ("ASU 2014-16"), which clarifies how to evaluate the economic characteristics and risk of a host contract in a hybrid financial instrument that is issued in the form of a share. In evaluating the nature of a host contract, an entity should assess the substance of the relevant terms and features (that is, the relative strength of the debt-like or equity-like terms and features given the facts and circumstances) when considering how to weight those terms and features. The effects of initially adopting ASU 2014-16 should be applied on a modified retrospective basis to existing hybrid financial instruments issued in a form of a share as of the beginning of the fiscal year for which the amendments are effective. Retrospective application is permitted to all relevant prior periods. ASU 2014-16 is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2015. Early adoption in an interim period is permitted. The Company does not expect the adoption of ASU 2014-16 to have a material impact on its financial statements.

In February 2015, the FASB issued ASU No. 2015-02, *Consolidation* (Topic 810)—*Amendments to the Consolidation Analysis* ("ASU 2015-02"), which changes the analysis that a reporting entity must perform to determine whether it should consolidate certain types of legal entities. These amendments are effective for fiscal years, and interim periods beginning after December 15, 2015. Early adoption is permitted. The Company does not expect the adoption of ASU 2015-02 to have a material impact on its financial statements.

In April 2015, the FASB issued ASU No. 2015-03, *Interest—Imputation of Interest* (Subtopic 835-30)—*Simplifying the Presentation of Debt Issuance Costs* ("ASU 2015-03"), which requires that debt issuance costs related to a recognized debt liability be presented in the balance sheet as a direct deduction from the carrying amount of that debt liability, consistent with debt discounts. The amendments in ASU 2015-03 are effective for financial statements issued for fiscal years beginning after December 15, 2015 and for annual and interim periods thereafter. Early adoption is permitted. The Company does not expect the impact of the adoption of ASU 2014-16 to have a material impact on its financial statements.

In November 2015, the FASB issued ASU No. 2015-17, *Income Taxes* (Topic 740)—*Balance Sheet Classification of Deferred Taxes* ("ASU 2015-17"), which requires that deferred tax liabilities and assets be classified as noncurrent in a classified statement of financial position, rather than separated into current and noncurrent amounts. This guidance is effective for financial statements issued for annual periods beginning after December 15, 2017, and interim periods within annual periods beginning after December 15, 2018. Early adoption is permitted. The Company has elected to early adopt ASU 2015-17 retrospectively in the fourth quarter of 2015. As a result, all deferred tax assets and liabilities have been presented as noncurrent in its consolidated balance sheets as of December 31, 2014 and 2015. There was no impact on the Company's consolidated statement of operations as a result of the adoption of ASU 2015-17.

In February 2016, the FASB issued ASU No. 2016-02, *Leases* ("ASU 2016-02"), which applies to all leases and will require lessees to record most leases on the balance sheet, but recognize expense in a manner similar to the current standard. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018 and interim periods within those years, which is the year ended December 31, 2019 for the Company. Entities are required to use a modified retrospective approach of adoption for leases that exist or are entered into after the beginning of the earliest comparative period in the financial statements. Full retrospective application is prohibited. The Company is evaluating the new guidance and the expected effect on its consolidated financial statements.

In March 2016, the FASB issued ASU No. 2016-09, Compensation—*Stock Compensation (Topic 718)* ("ASU 2016-09"). The guidance changes how companies account for certain aspects of equity-based payments to employees. Entities will be required to recognize income tax effects of awards in the income statement when the awards vest or are settled. The guidance also allows an employer to repurchase more of an employee's shares than it can under current guidance for tax withholding purposes providing for withholding at the employee's maximum rate as opposed to the minimum rate without triggering liability accounting and to make a policy election to account for forfeitures as they occur. The updated guidance is effective for annual periods beginning after December 15, 2017. Early adoption is permitted. The Company is currently evaluating the impact of the adoption of ASU 2016-09 on its consolidated financial position and results of operations.

3. Property and Equipment, net

The Company did not own any capital assets during the year ended December 31, 2014. Property and equipment, net, consists of the following (in thousands):

	As of December 31, 2015
Computer equipment and software	$ 118
Furniture, fixtures, and other	238
Laboratory equipment	861
Leasehold improvements	88
Construction work in process	95
	1,400
Accumulated Depreciation	(72)
Property and equipment, net	$ 1,328

Depreciation expense for the year ended December 31, 2014 and 2015 was $0 and $0.1 million, respectively.

4. Variable Interest Entities

TRACR Hematology Limited

On January 23, 2014, the founders of the Company formed TRACR in the United Kingdom, to further the development of the CRISPR/Cas9 technology into medicines for the treatment of blood-borne illnesses. On April 14, 2014, TRACR licensed certain foundational intellectual property rights under joint ownership from Dr. Emmanuelle Charpentier to develop and commercialize products for the treatment or prevention of human diseases related to hemoglobinopathies. See Note 9 for further details of the technology license agreement with Dr. Charpentier.

On April 14, 2014 the Company determined that it became the primary beneficiary of TRACR based on, among other factors, the Company's power to direct the activities that significantly impacted the economic performance of TRACR and the Company's financing of contractual obligations on behalf of TRACR, and the period in which the Company began to benefit from research and development of TRACR technology. Accordingly, the Company consolidated TRACR's financial statements as a consolidated VIE beginning on April 14, 2014.

The Company determined that TRACR met the definition of a business under the terms of ASC 805. As such, the Company accounted for the initial consolidation of TRACR as a business combination and measured the assets, liabilities and noncontrolling interests of TRACR in accordance with ASC 805 at the date the Company first became the primary beneficiary on April 14, 2014. The Company recorded $0.5 million of intangible assets on the Company's consolidated balance sheet for TRACR's intellectual property rights along with a related deferred tax liability of $0.1 million. TRACR did not have material operations prior to consolidation on April 14, 2014.

On March 24, 2015, the Company acquired 4,600 ordinary shares of TRACR, representing 82.1% of the ordinary share capital, pursuant to a share exchange transaction with the shareholders of TRACR. In exchange for 4,600 ordinary shares of TRACR and the assignment of certain rights to subscribe ordinary shares of TRACR, the Company issued 255,854 Common Shares to two founders of TRACR, 196,809 restricted Common Shares to certain employees and nonemployees, and 137,765 Common Shares to Fay Participation Corporation ("Fay Corp."), an entity formed to hold Common Shares for future issuance to certain employees and non-employees. As of December 31, 2015, the Company held 4,600 ordinary shares of TRACR, representing 82.1% of the ordinary share capital of TRACR.

Upon the share exchange on March 24, 2015, the Company recorded an adjustment of $0.1 million to decrease the carrying amount of the noncontrolling interest in TRACR and reflect the Company's increased ownership interest in TRACR's net assets. This adjustment was recognized directly in equity through additional paid-in capital and is attributable to the controlling interest. See Note 12 for further details.

Pursuant to the share exchange transaction on March 24, 2015, the Company also entered into a free standing call option agreement with Dr. Emmanuelle Charpentier for 1,000 ordinary shares of TRACR, representing the remaining 17.9% of the ordinary share capital of TRACR. Under the terms of the call option agreement, the Company has the option to acquire the remaining 1,000 shares of TRACR held by Dr. Charpentier in exchange for 98,405 Common Shares of the Company. In the event the option is exercised by the Company prior to a liquidation event, the Company will indemnify Dr. Charpentier for all taxes owed as a result of the exchange. In addition, upon a bankruptcy, liquidation, closing of an IPO, winding up of the Company, a change in control or other deemed liquidation event, as defined in the call option agreement, the remaining 1,000 ordinary shares of TRACR held by Dr. Charpentier will automatically convert into 98,405 Common Shares of the Company.

5. Intangible Assets

The Company's intangible assets consist of acquired intellectual property rights related to the Company's initial consolidation of TRACR in April 2014. Acquired intellectual property rights had an estimated life of 10 years. Intangible assets, net of accumulated amortization, are as follows:

Acquired intangible asset	Cost	Accumulated Amortization	Net
As of December 31, 2014	$547	$ (38)	$509
As of December 31, 2015	$547	$ (93)	$454

The Company recorded amortization expense of $38,000 and $0.1 million for the years ended December 31, 2014 and 2015, respectively. As of December 31, 2015, the remaining amortization period was 8.3 years. The Company has not recorded any impairment charges for the years ended December 31, 2014, and 2015. The estimated future amortization of acquired intangible assets as of December 31, 2015 is expected to be as follows (in thousands):

Year Ending December 31:	Amount
2016	$ 55
2017	55
2018	55
2019	55
2020	55
Thereafter	179
Total amortization	$ 454

6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	As of December 31, 2014	2015
Payroll and employee-related costs	$ 330	$ 773
Research costs	164	910
Licensing fees	—	1,055
Professional fees	236	2,412
Intellectual property costs	1,089	2,592
Other	105	688
Total	$1,924	$8,430

7. Convertible Loan

On October 26, 2015, the Company entered into a convertible loan agreement with Vertex and certain existing shareholders (the "Vertex Convertible Loan") under which the Company could borrow up to $40.0 million. The Vertex Convertible Loan accrues interest at 2.5% per annum and had an initial maturity date of April 26, 2016 subject to acceleration upon the occurrence of certain conditions stated in the loan agreement (the "Maturity Date"). On various dates between November 23 and December 7, 2015, the Company borrowed aggregate net proceeds of $38.2 million. The Vertex Convertible Loan included various embedded conversion, redemption and other features, as further described below, none of which required separate accounting from the host instrument under ASC 815. On January 29, 2016, all of the outstanding principal plus accrued interest of $0.2 million under the Vertex Convertible Loan was automatically converted into 857,783 Series B Preferred Shares in connection with a qualified financing. See Note 16 for further details of subsequent events.

An event of default ("Event of Default") is defined in the Vertex Convertible Loan Agreement and includes events of bankruptcy, insolvency or reorganization and, solely at the election of Vertex, a material breach that is not cured within the applicable notice and cure periods of the strategic collaboration, option and license agreement entered into by Vertex and the Company. See Note 9 for further details of the strategic, option and license agreement.

Conversion Terms

On the Maturity Date, the outstanding principal plus accrued interest automatically converts into Series B Preferred Shares at $31.084 per share.

In the event the Company issues equity securities prior to the Maturity Date with aggregate proceeds of not less than $50.0 million, of which $5.0 million is raised from investors other than Vertex or existing shareholders, the outstanding principal plus accrued interest under the Vertex Convertible Loan automatically converts into the newly issued equity securities at the price per share paid by the investors in the financing.

In the event of an underwritten public offering with shares of the Company listed on the New York Stock Exchange, the NASDAQ Global Market, or the NASDAQ Global Select Market, resulting in at least USD $50.0 million of proceeds to the Company ("IPO") closed prior to Maturity, the holders may elect, prior to the closing of the IPO, to convert the outstanding principal plus accrued interest into Series B Preferred Shares at $31.084 per share. Any Vertex Convertible Loan not converted prior to the closing of the IPO, shall automatically convert into Common Shares at a price paid by the investors for such shares in the IPO.

Upon a liquidation event prior to the Maturity Date, the holders may elect to convert the outstanding principal plus accrued interest into either Common Shares at a price of $31.084 per share or Series B Preferred Shares at a price of $31.084 per share.

Redemption Terms

Upon an Event of Default, all outstanding principal plus accrued interest becomes immediately due and payable.

Upon a liquidation event, if the holders do not exercise their conversion right, the outstanding principal plus accrued interest shall become due and payable in cash on the business day following the date on which the Company or its shareholders receive the proceeds from the liquidation event.

Contingent Interest

Upon an Event of Default, the outstanding amount of the Vertex Convertible Loan shall bear, in addition to the base interest of 2.5% per annum, default interest at a rate of 7.5% per annum.

8. Commitments and Contingencies

Operating Leases

The Company had five non-cancellable operating leases for office, laboratory, and corporate housing spaces during the year ended December 31, 2015. One of these leases expired in May 2015, and three other leases expire in 2016. The lease of the Company's primary research facility space expires in February 2022, with one optional five-year extension period. Rental expense for the years ended December 31, 2014 and 2015 was $17,000 and $1.3 million, respectively.

Future minimum payments required under the leases as of December 31, 2015, are as follows (in thousands):

Year Ending December 31:	Amount
2016	$1,291
2017	1,341
2018	1,381
2019	1,422
2020	1,465
Thereafter	1,700
Total minimum lease payments	$8,600

This table does not include $56.5 million of future minimum payments related to two leases for office and laboratory space entered into subsequent to December 31, 2015. See Note 16 for further details.

Letters of Credit

As of December 31, 2014 and 2015, the Company had restricted cash of $0.1 million and $0.7 million, respectively, representing letters of credit securing the Company's obligations under the facility lease in Cambridge, Massachusetts and certain credit card arrangements. The letters of credit are secured by cash held in a restricted depository account.

Sponsored Research Agreements

The Company has engaged several research institutions to identify new delivery strategies and applications of the CRISPR/Cas9 technology. As a result of these efforts, the Company has agreed to sponsor three research programs during 2016, with one of these programs continuing through 2018. In association with these agreements, the Company has committed to making payments for related research and development services of $1.2 million, $0.4 million, and $0.2 million in 2016, 2017, and 2018, respectively.

Licensing Agreements

In April 2014, the Company and TRACR entered into technology license agreements with Dr. Emmanuelle Charpentier pursuant to which the Company licensed Dr. Charpentier's interest to certain intellectual property rights jointly owned by Dr. Charpentier and others to develop and commercialize products for the treatment or prevention of human diseases. See Note 9 for further details.

Litigation

Under the Charpentier license agreement, the Company licenses a U.S. patent application that is currently subject to interference proceedings declared by the Patent Trial and Appeal Board of the U.S. Patent and Trademark Office. If the Company's licensed patent family does not prevail in these proceedings, claims could be asserted against the Company during development or commercialization of a product that relies on this technology. Defense of any such claims would involve substantial litigation expense, and any successful claim of infringement against the Company could require the Company to pay substantial damages.

9. Significant Contracts

Intellectual Property Agreements

CRISPR Therapeutics AG—Charpentier License Agreement

In April 2014, the Company entered into a technology license agreement with Dr. Emmanuelle Charpentier pursuant to which the Company licensed certain intellectual property rights under joint ownership from Dr.

Charpentier to develop and commercialize products for the treatment or prevention of human diseases other than hemoglobinopathies ("CRISPR—Charpentier License Agreement"). In consideration for the granting of the license, the Company paid Dr. Charpentier an upfront fee of CHF 0.1 million ($0.1 million), and agreed to pay an immaterial annual license maintenance fee if Dr. Charpentier is not otherwise engaged in a service arrangement with the Company. During the years ended December 31, 2014 and 2015, Dr. Charpentier has been in a consulting arrangement with the Company, as such, no annual payments have been made under this provision. Dr. Charpentier is entitled to receive nominal clinical milestone payments. The Company is also obligated to pay Dr. Charpentier a low single digit percentage of sublicensing payments received under any sublicense agreement with a third party. In addition, the Company is also obligated to pay to Dr. Charpentier a low single-digit percentage royalty based on annual net sales of licensed products and licensed services by the Company and its affiliates and sublicensees.

During the year ended December 31, 2015, the Company recorded $0.9 million of sublicensing fees due to Dr. Emmanuelle Charpentier in research and development expense under the terms of the CRISPR—Charpentier License Agreement that was triggered by the execution of the Vertex collaboration agreement.

TRACR Hematology Limited—Charpentier License Agreement

In April 2014, TRACR entered into a technology license agreement ("TRACR—Charpentier License Agreement") with Dr. Emmanuelle Charpentier pursuant to which TRACR licensed certain intellectual property rights under joint ownership from Dr. Charpentier to develop and commercialize products for the treatment or prevention of human diseases related to hemoglobinopathies. In consideration for the granting of the license, Dr. Charpentier is entitled to receive nominal clinical milestone payments. TRACR is also obligated to pay Dr. Charpentier a low single digit percentage of sublicensing payments received under any sublicense agreement with a third party. In addition, TRACR is obligated to pay to Dr. Charpentier low single digit percentage royalties based on annual net sales of licensed products and licensed services by the Company and its affiliates and sublicensees.

During the year ended December 31, 2015, the Company recorded $0.1 million of sublicensing fees due to Dr. Emmanuelle Charpentier in research and development expense under the terms of the TRACR—Charpentier License Agreement that was triggered by the execution of the Vertex collaboration agreement.

Patent Assignment Agreement

In November 2014, the Company entered into a patent assignment agreement ("Patent Assignment Agreement") with Dr. Emmanuelle Charpentier, Dr. Ines Fonfara, and the University of Vienna (collectively, the "Assignors"), pursuant to which the Company was assigned all rights, title and interest in and to certain patent rights claimed in the U.S. Patent Application No.61/905,835. In consideration for the assignment of such rights, the Assignors are entitled to receive clinical milestone payments totaling up to €0.3 million (approximately $0.4 million) in the aggregate for the first human therapeutic product. The Company is also obligated to pay to the Assignors low single digit royalties based on annual net sales of licensed products and licensed services by the Company and its affiliates and sublicensees.

During the year ended December 31, 2015, the Company recorded $0.1 million of sublicensing fees due to the Assignors in research and development expense under the terms of the Patent Assignment Agreement that was triggered by the execution of the Vertex collaboration agreement.

Collaboration Agreement with Vertex Pharmaceuticals, Incorporated

Summary of Agreement

On October 26, 2015, the Company entered into a strategic collaboration, option, and license agreement ("Collaboration Agreement") with Vertex, focused on the use of CRISPR's gene editing technology, known as

CRISPR/Cas9, to discover and develop potential new treatments aimed at the underlying genetic causes of human disease. The collaboration will evaluate the use of CRISPR-Cas9 across multiple diseases where targets have been validated through human genetics. Vertex and CRISPR will focus their initial gene editing research on discovering treatments to address the mutations and genes known to cause and contribute to sickle cell disease, beta-thalessemia and cystic fibrosis. Vertex and CRISPR will also evaluate a specified number of other genetic targets as part of the collaboration. For up to six targets, Vertex has an exclusive option to obtain: (1) an exclusive license to commercialize CRISPR technology ("Exclusive License") or (2) a co-exclusive license with respect to hemoglobinopathy and beta-globin targets ("Co-exclusive License").

The collaborative program of research to be undertaken by the parties pursuant to the Collaboration Agreement will be conducted in accordance with a mutually agreed upon research plan which outlines each party's research and development responsibilities across the three research areas. The Company's research and development responsibilities under the research plan ("R&D services") are related to generating genome editing reagents that modify gene targets selected by Vertex. Except with respect to the Company's obligations under the mutually agreed upon research plan, Vertex has sole responsibility, at its own costs, for the worldwide research, development, manufacturing and commercialization of products resulting from the exclusive licenses obtained.

The research collaboration will end on the earlier of the date on which Vertex has exercised six options to obtain exclusive/co-exclusive licenses with respect to a collaboration target, or the fourth anniversary of the effective date of the agreement. The research term may be extended as mutually agreed by the parties up to nine additional months to complete any research activities under the approved research plan that are incomplete on the fourth anniversary of the effective date.

The Collaboration Agreement will be managed on an overall basis by a project leader from each of the Company and Vertex. In addition, the activities under the collaboration agreement during the research term will be governed by a joint research committee ("JRC") formed by an equal number of representatives from the Company and Vertex. Decisions by the JRC will be made by consensus of the group, however, Vertex will have final decision-making authority in the event of disagreement, provided it is in good faith and not contrary to any explicit clause of the agreement.

In connection with the agreement, Vertex made a nonrefundable upfront payment of $75.0 million. In addition, Vertex will fund all of the discovery activities conducted pursuant to the agreement. For potential hemoglobinopathy treatments, including treatments for sickle cell disease, the Company and Vertex will share equally all research and development costs and worldwide revenues. For other targets that Vertex elects to license, Vertex would lead all development and global commercialization activities. For each of up to six targets that Vertex elects to license, other than hemoglobinopathy targets, the Company has the potential to receive up to $420.0 million in development, regulatory and commercial milestones and royalties on net product sale.

Vertex is entitled to terminate the Collaboration Agreement as a whole, or terminate the Collaboration Agreement in part with respect to a particular collaboration program, for convenience by providing the Company 90 days' written notice of such termination; provided, however, that if any termination applies to a product for which Vertex has received marketing approval, Vertex will provide CRISPR no less than 270 days' notice of such termination. If Vertex is in material breach of this Collaboration Agreement, the Company has the right to terminate the Collaboration Agreement in full at its discretion 90 days after delivery of written notice to Vertex.

The Company evaluated the Collaboration Agreement in accordance with the provisions of ASC 605-25. The Company's arrangement with Vertex contains the following initial deliverables: (i) a non-exclusive research license; (ii) the option to obtain an exclusive license for up to six Collaboration Targets; (iii) the option to obtain a co-exclusive license for hemoglobinopathy or beta-globin targets (which would be included within the maximum number of the aforementioned six collaboration targets); (iv) R&D Services; and (v) JRC participation.

Management considered whether any of these deliverables could be considered separate units of accounting. Regarding the non-exclusive research license, the Company concluded that it does not have stand-alone value separate from the option to exercise the exclusive or co-exclusive license since Vertex would not benefit from acquiring a research license without the ability to obtain the license to commercialize the results of that research. As a result, the Company concluded that the research license should be combined with those options.

Regarding the R&D Services, the Company concluded that there are other vendors in the market that could perform the related services. As such the Company concluded the R&D Services represent a separate unit of accounting.

Regarding the JRC obligations, the Company concluded that the JRC obligations deliverable has standalone value from the option to license because the services could be performed by an outside party. As such the Company concluded the JRC obligations represent a separate unit of accounting.

As a result, management concluded that there are four units of accounting at the inception of the agreement: (i) a combined unit of accounting representing the non-exclusive research license, and the option for up to six exclusive licenses to develop and commercialize the collaboration targets as these options do not have stand-alone value; (ii) a combined unit of accounting representing the non-exclusive research license, and the option for a co-exclusive license (subject to the aforementioned six license limit) to develop and commercialize the hemoglobinopathy or beta-globin targets as these options do not have stand-alone value; (iii) the performance of R&D Services; and (iv) the participation in the JRC.

The Company has determined that neither VSOE of selling price nor TPE of selling price is available for any of the units of accounting identified at inception of the arrangement. Accordingly, the selling price of each unit of accounting was determined based on the Company's BESP. The Company developed the BESP for all of the units of accounting included in the collaboration agreement with the objective of determining the price at which it would sell such an item if it were to be sold regularly on a standalone basis.

The Company developed the BESP for the R&D Services and the JRC participation primarily based on the nature of the services to be performed and estimates of the associated effort and cost of the services, adjusted for a reasonable profit margin that would be expected to be realized under similar contracts. The Company's BESP for the R&D Services was $21.4 million. The Company's BESP for the JRC participation services was de minimis based on an estimate of time spent on preparation, participation, review and travel for the meetings.

The Company's BESP for each combined unit of the non-exclusive research license and the option for an exclusive license to develop and commercialize a single collaboration target is $37.7 million. As the Company expects Vertex to exercise five of these options, the total BESP is $188.5 million. BESP for this item was determined based on probability and present value adjusted cash flows from the royalties and milestones outlined in the Collaboration Agreement. BESP reflects the level of risk and expected probability of success inherent in the nature of the associated research area.

The Company's BESP for a non-exclusive research license and the option for a co-exclusive license to develop and commercialize a single hemoglobinopathy or beta-globin collaboration target is $12.5 million. As the Company expects Vertex to exercise one of these options, the total BESP is $12.5 million. BESP for this item was determined based on probability and present value adjusted cash flows from the equal sharing of project worldwide net profit or net loss. BESP reflects the level of risk and expected probability of success inherent in the nature of the associated research area.

Allocable arrangement consideration at inception is comprised of: (i) the up-front payment of $75.0 million, (ii) the estimated R&D services of $21.4 million and (iii) payments related to the estimated exercise of options on future exclusive licenses for five targets of $50.0 million. The aggregate allocable arrangement consideration of $146.4 million was allocated among the separate units of accounting using the relative selling price method as

follows: (i) R&D Services: $14.1 million, (ii) non-exclusive research license, and the option for an Exclusive License to develop and commercialize the five collaboration targets: $124.1 million, (iii) non-exclusive research license, and the option for one Co-exclusive License to develop and commercialize one hematology target: $8.2 million.

The amount allocated to R&D Services will be recognized as the R&D Services are performed. The Company will recognize as license revenue an equal amount of the total arrangement consideration allocated to the exclusive licenses as each individual license is delivered to Vertex upon Vertex's exercise of its options to such licenses. The Company will recognize $8.2 million as license revenue when the Co-exclusive License is delivered to Vertex upon Vertex's exercise of its options to such license.

The Company has evaluated all of the milestones that may be received in connection with the Collaboration Agreement. In evaluating if a milestone is substantive, the Company assesses whether: (i) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the Company's performance to achieve the milestone, (ii) the consideration relates solely to past performance, and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. As the first milestone of the agreement relates to the exercise of an exclusive option by Vertex to obtain an Exclusive License to commercialize CRISPR/Cas9 technology, the Company has considered it to be substantive. Accordingly, such amounts will be recognized as revenue in full in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. The next potential milestone the Company will be entitled to receive will be a $10 million milestone due upon the exercise of the first Exclusive License.

The remainder of the milestones are predominately related to the development and commercialization of a product resulting from the arrangement. After Vertex has exercised an Exclusive License option, Vertex will be solely responsible for all research, development, manufacturing, and commercialization of licensed agents and products for the relevant target. As the Company's involvement in this process is limited to observer status, management determined that milestones are not considered substantive because they do not relate solely to the past performance of the Company. Upon the achievement of a milestone, management will evaluate whether the triggering event occurs during or after the research term. If the triggering event occurs during the research term, management has elected to treat the milestone similar to an up-front payment. In these cases, if and when any of these milestones are received, the amount will be included in the overall arrangement consideration and allocated to the remaining identified deliverables. To the extent all deliverables have been satisfied, any additional consideration allocated to them could be immediately recognized. If the triggering event occurs after the research term, the Company will recognize the associated revenue in the period in which the event occurs. The Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

During the year ended December 31, 2015, the Company recognized $0.2 million of revenue with respect to the collaboration with Vertex. Research and development expense incurred by the Company in relation to its performance under the Collaboration Agreement for the year ended December 31, 2015 was $0.3 million. As of December 31, 2015, there is $75.1 million of non-current deferred revenue related to the Company's collaboration with Vertex.

Joint Venture with Bayer Healthcare LLC

On December 19, 2015, the Company entered into an agreement to establish a joint venture ("Bayer Joint Venture") with Bayer Healthcare LLC ("Bayer") to discover, develop and commercialize new therapeutics to cure blood disorders, blindness, and congenital heart disease. The joint venture was formed in February 2016, see Note 16 for further details.

Subscription Agreement with Bayer Global Investments B.V.

On December 19, 2015, the Company entered into a subscription agreement, ("Subscription Agreement"), with Bayer Global Investments B.V., ("Bayer BV"). Pursuant to the Subscription Agreement, Bayer BV was given the option, at its election, to purchase up to $35.0 million of the Company's Common Shares in a private placement concurrent with the Company's IPO at a per share price equal to the public offering price, see Note 16 for further details.

10. Redeemable Convertible Preferred Shares

As of December 31, 2015, the Company had 5,651,105 registered Preferred Shares issued and outstanding in share capital, which was comprised of (i) 132,000 Series A-1 Preferred Shares CHF 0.10 par value per share; (ii) 936,000 Series A-2 Preferred Shares, CHF 0.10 par value per share; (iii) 3,227,401 Series A-3 Preferred Shares, CHF 0.10 par value per share; and, (iv) 1,355,704 Series B Preferred Shares, CHF 0.10 par value per share, (collectively, the "Preferred Shares").

The Company's redeemable convertible preferred shares have been classified as temporary or mezzanine equity on the accompanying consolidated balance sheets in accordance with authoritative guidance for the classification and measurement of redeemable securities as the Preferred Shares are contingently redeemable at the option of the holders.

In October 2013, the Company issued 132,000 Series A-1 Preferred Shares for CHF 3.80 ($4.25) per share, resulting in gross proceeds of CHF 0.5 million ($0.6 million). Under the terms of the Series A-1 Preferred Shares Investment Agreement, the holders had the right to purchase an additional 394,737 Series A-1 Preferred Shares at CHF 3.80 ($4.25) per share (the "Series A-1 Tranche Rights") contingent upon two or more shareholders holding Series A-1 Preferred Shares. These rights were not legally detachable. The Series A-1 Tranche Rights were evaluated under ASC 480 and ASC 815 and it was determined that they did not meet the requirements for separate accounting from the initial issuance of Series A-1 Preferred Shares. In connection with the issuance of the Series A-1 Preferred Shares, the Company also issued 100,500 Common Shares to the Series A Preferred Shares investors. The Company recorded the difference of $0.1 million between the fair value of the Common Shares issued and the price paid by the investors as an issuance cost discount to the Series A-1 Preferred Shares upon issuance. See Note 11 for further details.

In April 2014, the Company issued 936,000 Series A-2 Preferred Shares in exchange for CHF 10.162 ($11.57) per share of such amount CHF 4.82 ($5.49) per share was received upon issuance resulting in gross proceeds of CHF 4.5 million ($5.1 million) and the balance of CHF 5.342 ($6.08) per share was called in February 2015 by the Board of Directors of the Company resulting in additional gross proceeds of CHF 5.0 million ($5.3 million).

In connection with the issuance of the Series A-2 Preferred Shares, the Series A-1 Tranche Rights were terminated without exercise in April 2014. The Company's policy requires the evaluation of amendments to preferred shares qualitatively to determine whether they are considered a modification or extinguishment. Based on this approach, the amendment to the terms of the Series A-1 Preferred Shares was considered an extinguishment due to the significance of the modifications to the substantive contractual terms of the Series A-1 Preferred Shares. Accordingly, the Company recorded a loss of $0.7 million on the Series A-1 Preferred Shares within additional paid-in capital equal to the difference between the fair value of the Series A-1 Preferred Shares of $1.2 million and the carrying amount of the Series A-1 Preferred Shares of $0.4 million upon extinguishment. The loss on extinguishment is reflected in the calculation of net loss available to common stockholders in accordance with FASB ASC Topic 260, *Earnings per Share* ("ASC 260").

In April 2015, the Company issued 3,227,401 Series A-3 Preferred Shares in exchange for $14.16 per share whereby $7.08 per share was received upon issuance, resulting in gross proceeds of $22.8 million and the

balance of $7.08 per share was due upon meeting certain milestones. As of December 31, 2015, none of the milestones had occurred and the Company had an outstanding subscription receivable of $22.8 million related to the Series A-3 Preferred Shares. In connection with the issuance of the Series A-3 Preferred Shares, the Company amended the dividend and conversion terms of the Series A-1 and Series A-2 Preferred Shares. The Company's policy requires the evaluation of amendments to equity classified preferred shares qualitatively to determine whether they are considered a modification or extinguishment. Based on this approach, the amendment to the terms of the Series A-1 and A-2 Preferred Shares was considered a modification and as a result, there was no adjustment to the carrying value of the Series A-1 and A-2 Preferred Shares. The balance of the Series A-3 Preferred Share subscription receivable of $7.08 per share was called on May 5, 2016 by the Board of Directors. See Note 16 for further details.

In May 2015, the Company issued 1,355,704 Series B Preferred Shares in exchange for CHF 20.6535 ($22.47) per share resulting in gross proceeds of CHF 28.0 million ($30.5 million).

Redemption

The Preferred Shares may be redeemed upon written election of the holders of 66.7% of the Preferred Shares. The Series B Preferred Shares, Series A-3 Preferred Shares, Series A-2 Preferred Shares and Series A-1 Preferred Shares may be redeemed at CHF 20.6535, $7.08, CHF 10.162 and CHF 3.80 per share, respectively, or the Series B Preferred Shares, Series A-3 Preferred Shares, Series A-2 Preferred Shares and Series A-1 Preferred Shares may receive an amount equal to the amount entitled if the Preferred Shares converted into shares of Common Shares on a one-for-one basis on the redemption date. At December 31, 2015, the Series A-3 Preferred Shares are redeemable up to the amount paid in prior to the receipt of the payment of the Series A-3 Preferred Shares subscription receivable. Upon receipt of the payment of the Series A-3 Preferred Shares subscription receivable in 2016, the Series A-3 Preferred Shares may be redeemed at $14.16.

Conversion

Preferred Shares are convertible into Common Shares initially on a one-for-one basis, subject to adjustment for share splits, share dividends, combination of shares, reorganization, recapitalization, reclassification, or similar events.

The Preferred Shares automatically convert into Common Shares at the then applicable conversion rate, upon either (i) the consent of at least 66.7% of the then outstanding Preferred Shares, voting as a separate class; or (ii) upon the closing of a firmly underwritten IPO of the common shares that is (A) pursuant to a registration statement under the Securities Act of 1933, as amended, (B) with aggregate proceeds of at least $50.0 million before deduction of underwriter expenses or commissions, (C) at a per share public offering price greater than two times the Series A-3 Original Issue Price (as adjusted for share splits, share dividends, combination of shares, reorganization, recapitalization, reclassification, or similar event) and (D) with the shares of the Company listed on the New York Stock Exchange, the NASDAQ Global Market, or the NASDAQ Global Select Market ("QPO").

The Series B, Series A-2 and Series A-1 Preferred Shares are convertible to Common Shares at the holders' option at any time, at the applicable conversion rate. The Series A-3 Preferred Shares are convertible to Common Shares at the holder's option subsequent to the receipt of the payment of the Series A-3 Preferred Shares subscription receivable.

The Series A-3 Preferred Shares are automatically converted to Common Shares at a rate of ten Series A-3 Preferred Shares for each Common Share if the payment of the Series A-3 Preferred Shares subscription receivable is not made timely when called by the Board of Directors of the Company. The balance of the Series A-3 Preferred Share subscription receivable of $7.08 per share was called on May 5, 2016 by the Board of Directors. The Series A-3 Preferred Shares will automatically convert under this provision if payment is not made on or before June 17, 2016. See Note 16 for further details.

Dividends

The holders of Preferred Shares are entitled to receive non-cumulative dividends, when and if declared by the Board of Directors, on a pari passu basis prior and in preference to the holders of the Common Shares at a rate of 8% per annum of the original issuance price, subject to adjustment for additional capital contributions. The holders of Preferred Shares shall participate pro rata in any dividends paid on the Common Shares on an as-converted to Common Shares basis.

Liquidation Preference

Upon a liquidation event, after all debts of the Company have been paid, the remaining net proceeds shall be distributed pari passu to the holders of Preferred Shares until they have received the amount paid upon issuance plus any subsequent contributions made into the legal capital reserve of the Company. If upon a liquidation event, the assets of the Company legally available for distribution to the preferred shareholders is insufficient to pay the full amounts, then the entire assets of the Company legally available for distribution shall be distributed with equal priority and pro rata among the holders of the Preferred Shares in proportion to the full amounts they would otherwise be entitled to receive. After the payment of the liquidation rights to the holders of Preferred Shares, the remaining assets of the Company are to be distributed with equal priority and pro rata among the holders of the Common Shares in proportion to the number of shares held.

Anti-Dilution Protection

In the event of future capital increases, the holders of the Series B and A-3 Preferred Shares are irrevocably entitled to newly issued Preferred Shares at their nominal value to compensate for their dilution, if any, between the subscription price of the new shares and the price previously paid for the Preferred Shares. The Board of Directors shall determine the number of new Series B and A-3 Preferred Shares to be issued in such a case at par value. The same procedure shall apply in the event of stock splits, reverse stock splits, stock dividends, or similar transactions.

Voting Rights

Except for matters with specific voting rights, the holders of Preferred Shares vote together with the holders of the Common Shares as a single class on any matter presented to the shareholders of the Company for their action or consideration at any meeting of the shareholders of the Company or by written consent of the shareholders in lieu of meetings. The holders of the Preferred Shares are entitled to the number of votes equal to the number of Common Shares into which each of the Preferred Shares are convertible at the time of such vote, initially on a one-for-one basis. A vote of 66.7% of the Preferred Shareholders, voting as a single class, is required for certain matters, including any change to the Company's Articles of Association or number of Directors. In addition, the holders of Preferred Shares have the right to designate five (5) of the eight (8) members of the Board of Directors.

11. Share Capital

As of December 31, 2015, the Company had 1,658,428 registered Common Shares and 5,651,105 registered Preferred Shares outstanding with a par value of CHF 0.10 per share in share capital.

Conditional Capital

Since inception, the Company has created conditional capital for the establishment of its 2015 option and grant plan (the "2015 Plan"), shares issuable under the terms of the call option agreement with Dr. Emmanuelle Charpentier, and Preferred Shares issuable under the terms of the convertible loan financings. As of December 31, 2015, the Company had conditional capital which would enable an increase in its share capital of up to 733,309 registered Common Shares with a par value of CHF 0.10 per share, which was comprised of

(i) 634,904 Common Shares for grants under the 2015 Plan and (ii) 98,405 Common Shares for issuance under the terms of the call option agreement with Dr. Charpentier. See Note 4 for further details of the call option agreement with Dr. Charpentier.

In January 2016, the Company created additional conditional capital which would enable an increase in its share capital of up to 2,291,206 Series B Preferred Shares, with a par value of CHF 0.10 per share, issuable under certain terms of the convertible loans. On January 29, 2016, the convertible loans converted and 1,639,382 Series B Preferred Shares moved from conditional capital to issued share capital. See Note 16 for further details of the conversion of convertible loans in January 2016.

In April 2016, the Company created additional conditional capital which would enable an increase in its share capital of up to 272,000 Common Shares, with a par value of CHF 0.10 per share, for future grants under the 2015 Plan. See Note 12 for further details of the 2015 Plan.

Conditional Capital Reserved for Future Issuance

The Company had the following conditional capital reserved for future issuance:

		As of December 31,	
Type of Share Capital	**Conditional Capital**	**2014**	**2015**
Common Shares	Charpentier Call Option	—	98,405
Common Shares	Unvested restricted share awards under 2015 Plan	—	42,838
Common Shares	Outstanding stock options awards under 2015 Plan	—	581,999
Common Shares	Reserved for future issuance under the 2015 Plan	—	10,067
	Total	—	733,309

Common Share Issuances

In October 2013, the Company issued 774,000 Common Shares to its founders (“Founders’ Shares”) and 100,500 Common Shares to its investors for CHF 87,450. In December 2013, the Company issued an additional 193,500 Common Shares to two investor directors in exchange for total proceeds of CHF 19,350, which was recorded as a Common Shares subscription receivable until April 2014, when cash proceeds were received. The Company recorded the difference between the fair value of the Common Shares issued and the price paid by the investors as an issuance cost discount to the Series A-1 Preferred Share issuance in October 2013. The Company recorded the difference between the fair value of the Common Shares issued and the price paid by the founders and directors as equity-based compensation expense. See Note 12 for further details of equity-based compensation related to these Common Share issuances.

In April 2014, in conjunction with the sale of its Series A-2 Preferred Shares, the Company and its founders agreed to transfer 218,940 Founders’ Shares to several non-employees. The shares transferred were subject to service-based vesting conditions. If the holder of any restricted Common Shares terminates the service relationship, the unvested shares are subject to a right of repurchase at an escalating purchase price. Both vested and unvested shares are subject to a right of repurchase at the original purchase price upon certain triggering events such as termination for cause, material breach of agreement, and insolvency of the holder. In addition, the founders and an investor also agreed to transfer 357,780 fully vested Common Shares to Fay Corp. The Company recorded equity-based compensation expense for the Founders Shares and the Common Shares issued with vesting restrictions from the founders and Fay Corp. See Note 12 for further details of equity-based compensation related to these transfers.

In March 2015, the Company entered into an agreement to acquire 82.1% of the ordinary share capital of TRACR in a share exchange transaction. In connection with this share exchange transaction, the Company issued 255,854 Common Shares to two founders of TRACR, 137,765 Common Shares to Fay Corp. and 196,809

restricted Common Shares to certain employee and non-employee advisors of TRACR. If the holders of any restricted common shares terminates the service relationship the unvested shares are subject to a right of repurchase at an escalating purchase price. If any of these holders of restricted Common Shares are terminated, in certain circumstances, the vested and unvested shares are subject to a right of repurchase at the shareholder's original purchase price. The Company recorded equity-based compensation expense in April 2015 for the incremental value received by the holders in exchange for the vested TRACR shares as of the exchange date. The Company is also recognizing additional equity-based compensation expense for the exchange of TRACR restricted share awards which will continue to vest over a remaining term in the form of CRISPR restricted share awards. See Note 12 for further details of equity-based compensation related to this share exchange transaction.

Pursuant to the share exchange transaction on March 24, 2015, the Company also entered into a free standing call option agreement with Dr. Emmanuelle Charpentier for 1,000 ordinary shares of TRACR, representing the remaining 17.9% of the ordinary share capital of TRACR. Under the terms of the call option agreement the Company has the option to acquire the remaining 1,000 ordinary shares of TRACR held by Dr. Charpentier in exchange for 98,405 Common Shares. In addition, upon a bankruptcy, liquidation, closing of an IPO, winding up of the Company, a change in control or other deemed liquidation event, as defined in the agreement, the remaining 1,000 ordinary shares of TRACR held by Dr. Charpentier automatically convert into 98,405 Common Shares of the Company. See Note 4 for further details of the call option agreement.

For the year ended December, 31, 2015, the Company has determined that it is considered a passive foreign investment company. Under the terms of a shareholder agreement, if a U.S. common shareholder elects to file a Qualified Electing Fund ("QEF") and notifies the Company of this election, the Company is required to make advance payments to the shareholder related to their individual 2015 tax liability. The Company estimates that it may be required to make advance payments up to $2.3 million for the tax year ended December 31, 2015 if notified by shareholders of a QEF election. As no notifications have been made, the Company has not paid or accrued any amounts as of December 31, 2015. The obligation to make advance payments under the shareholder agreement will terminate upon the closing of an IPO.

The voting, dividend and liquidation rights of the holders of Common Shares are subject to and qualified by the rights, powers and preferences of the holders of Preferred Shares. The Common Shares have the following characteristics:

Voting Rights

The holders of Common Shares are entitled to one vote for each Common Share held at all meetings of shareholders and written actions in lieu of meetings.

Dividends

The holders of Common Shares are entitled to receive dividends, if and when declared by the Board of Directors. As of December 31, 2015, no dividends have been declared or paid since the Company's inception.

Liquidation

After payment to the holders of Preferred Shares of their liquidation preferences, the holders of the Common Shares are entitled to share ratably in the Company's assets available for distribution to shareholders in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or upon the occurrence of a deemed liquidation event.

12. Equity-based Compensation

2015 Option and Grant Plan

In April 2015, the shareholders approved the 2015 Plan. The 2015 Plan provides for the issuance of equity awards in the form of restricted shares, options to purchase Common Shares which may constitute incentive

stock options (“ISOs”) or non-statutory stock options (“NSOs”), unrestricted stock unit grants, and qualified performance-based awards to eligible employees, officers, directors, consultants, and other key personnel. Terms of the equity awards, including vesting requirements, are determined by the Board, subject to the provisions of the Plan. Options granted by the Company typically vest over four years and have a contractual life of ten years. As of December 31, 2015, no options were exercised and there were 581,999 options and 42,838 restricted shares outstanding under the 2015 Plan. As of December 31, 2015, the Company had 10,067 Common Shares reserved for future grant under the 2015 Plan.

As of December 31, 2015, the Company had conditional capital which would enable an increase in its share capital of up to 634,904 registered Common Shares with a par value of CHF 0.10 per share for grants under the 2015 Plan. In April 2016, the Company created additional conditional capital which would enable an increase in its share capital of up to 272,000 Common Shares, with a par value of CHF 0.10 per share, for future grants under the 2015 Plan.

Prior to the adoption of the 2015 Plan, certain employees and non-employees were granted restricted Common Shares directly from the Company and from a pool of unrestricted Common Shares held by the founders and Fay Corp. Such shares are treated as issued and outstanding Common Shares by the Company in all periods presented.

Equity-based Compensation Expense

Total equity-based compensation expense is recognized for stock options and restricted shares granted to employees and non-employees and has been reported in the Company’s consolidated statements of operations as follows (in thousands):

	Year Ended December 31,	
	2014	2015
Research and development	$ 487	$ 1,924
General and administrative	208	1,760
Total	$ 695	$ 3,684

Stock Option Awards

The following table summarizes stock option activity for employees and non-employees (intrinsic value in thousands):

	Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value
Outstanding at December 31, 2014	—			
Granted	581,999	$ 7.70		
Exercised	—			
Cancelled or forfeited	—			
Outstanding at December 31, 2015	581,999	$ 7.70	9.7	$ 6,688
Exercisable at December 31, 2015	73,077	$ 6.25	9.7	$ 946
Vested or expected to vest at December 31, 2015(1)	517,204	$ 7.73	9.7	$ 5,927

(1) Represents the number of vested options at December 31, 2015 plus the number of unvested options expected to vest based on the unvested options outstanding at December 31, 2015.

There were no stock options granted during the year ended December 31, 2014. During the year ended December 31, 2015, the Company granted stock options to purchase an aggregate of 581,999 Common Shares with a weighted-average grant date fair value of $10.44. The expense related to options granted to employees and non-employees was $1.1 million and $33,000, respectively, for the year ended December 31, 2015.

As of December 31, 2015, no stock options have been exercised, cancelled or forfeited. As of December 31, 2015, the total unrecognized compensation cost related to employee, non-vested stock options granted under the 2015 Plan was $4.2 million. As of December 31, 2015, the total unrecognized compensation cost related to non-employee, non-vested stock options granted under the 2015 Plan was $0.1 million.

The total unrecognized compensation cost for employee and non-employee awards will be adjusted for future forfeitures. The Company expects to recognize total unrecognized compensation cost over a remaining weighted-average period of 3.3 years.

The Company estimates the fair value of each employee and non-employee stock award on the grant date using the Black-Scholes option-pricing model based on the following range of assumptions regarding the fair value of the underlying Common Shares on each measurement date:

	Year Ended December 31, 2015
Employees:	
Weighted average expected volatility	76.4%
Expected term (in years)	6.0
Risk free interest rate	1.7 - 1.9%
Expected dividend yield	0.0%
Non employees:	
Weighted average expected volatility	83.3 - 84.2%
Expected term (in years)	10.0
Risk free interest rate	2.1 - 2.3%
Expected dividend yield	0.0%

During 2015, the Company granted options to purchase 16,085 Common Shares subject to service and performance-based vesting conditions. At December 31, 2015, none of these options were vested, however, options to purchase 16,085 Common Shares were deemed probable of vesting.

During 2015, the Company granted options to purchase 62,332 Common Shares subject to performance-based vesting conditions. As of December 31, 2015, options to purchase 27,052 Common Shares with performance-based vesting conditions were vested, as performance conditions were achieved, and options to purchase 8,290 Common Shares were deemed probable of vesting.

Restricted Share Awards

From time to time, upon approval by the Board of Directors, certain employees and non-employees have been granted restricted Common Shares. These restricted shares are subject to certain transfer restrictions and repurchase rights. Accordingly, the Company has recorded proceeds, if any, from the issuance of restricted shares as a liability in the balance sheets included as a component of accrued expenses or other long term liabilities based on the scheduled vesting dates. The restricted share liability is reclassified into shareholders' (deficit) equity as the restricted shares vest.

During the year ended December 31, 2015, the Company issued 196,809 restricted Common Shares pursuant to the TRACR share exchange transaction. These restricted Common Shares were registered with the Swiss commercial register in April 2015 and are treated as issued and outstanding Common Shares by the Company in all periods presented. During the year ended December 31, 2015, the Company issued 42,838 restricted shares under the 2015 Plan. These restricted Common Shares are reserved for future issuance in conditional capital under the 2015 Plan. A summary of the status of and changes in unvested restricted Common Shares as of December 31, 2014 and 2015 is as follows:

	Shares	Weighted-Average Grant Date Fair Value per Share
Unvested Restricted Common Shares as of December 31, 2014	—	$ —
Issued	239,647	$ 7.06
Vested	(120,272)	$ 6.98
Unvested Restricted Common Shares as of December 31, 2015	119,375	$ 7.13

There were no restricted share awards issued directly by the Company to employees and non-employees in the year ended December 31, 2014. The expense related to restricted share awards granted directly by the Company to employees and non-employees was $0.1 million and $0.4 million, respectively, for the year ended December 31, 2015.

As of December 31, 2015, the Company had unrecognized equity-based compensation expense related to its employee unvested restricted share awards of $0.3 million. As of December 31, 2015, the Company had unrecognized equity-based compensation expense related to its non-employee unvested restricted share awards of $1.2 million.

The total unrecognized compensation cost for employee and non-employee awards will be adjusted for future forfeitures. The Company expects to recognize total unrecognized compensation cost over a remaining weighted-average period of 2.4 years.

The fair value of employee restricted share awards vested during the year ended December 31, 2015, based on estimated fair values of the shares underlying the restricted share awards on the day of vesting, was $0.1 million. The fair value of non-employee restricted share awards vested during the year ended December 31, 2015, based on estimated fair values of the shares underlying the restricted share awards on the day of vesting, was $0.8 million.

In September 2015, a certain executive purchased $0.2 million of Common Shares for CHF 6.00 per share. These shares are subject to certain transfer restrictions and repurchase rights which lapse as the shares vest over a requisite service period, which allow the Company in certain circumstances where the holder's employment is terminated to repurchase the shares from the employees at the lower of initial purchase price or fair market value. As a result of these repurchase features, the Company has determined the proceeds the Company received for these shares should be recorded as a restricted stock liability until the shares have vested.

Founders Shares Awards

In October 2013, the Company issued 774,000 Founders' Shares and 100,500 Common Shares to its investors in exchange for total proceeds of CHF 87,450. In December 2013, the Company issued an additional 193,500 Common Shares to two directors in exchange for total proceeds of CHF 19,350, which was recorded as a Common Share subscription receivable until April 2014, when cash proceeds were received. The Company recorded the difference between the fair value of the Common Shares issued and the price paid by the founders and directors as equity-based compensation expense in the year ended December 31, 2013.

In April 2014, in conjunction with the sale of its Series A-2 Preferred Shares, the Company and its founders agreed to transfer 218,940 Founders' Shares to certain employee and non-employee advisors. The shares transferred were subject to service-based vesting conditions. If the holder of any restricted Common Shares terminates the service relationship, the unvested shares are subject to a right of repurchase at an escalating purchase price. Both vested and unvested shares are subject to a right of repurchase held by Fay Corp. at the original purchase price upon certain triggering events such as termination for cause, material breach of agreement, and insolvency of the holder. A summary of the status of and changes in unvested restricted shares transferred as of December 31, 2014 and December 31, 2015 is as follows:

	Shares	Weighted-Average Grant Date Fair Value per Share
Unvested Common Shares transferred from Founders' Shares as of December 31, 2013	—	$ —
Transferred	218,940	$ 5.04
Vested	(54,735)	$ 5.04
Unvested Common Shares transferred from Founders' Shares as of December 31, 2014	164,205	$ 5.04
Vested	(79,061)	$ 5.04
Unvested Common Shares transferred from Founders' Shares as of December 31, 2015	85,144	$ 5.04

The Company recorded equity-based compensation expense for the Common Shares issued with vesting restrictions from the founders to the employee and non-employee advisors as the awards represented compensation for services to be performed for the benefit of the Company. The expense related to the Common Shares transferred from the pool of Founder's Shares to employees and nonemployees with vesting restrictions was $0 and $0.5 million, respectively, for the year ended December 31, 2014. The expense related to the Common Shares transferred from the pool of Founder's Shares to employees and nonemployees with vesting restrictions was $19,000 and $0.5 million, respectively, for the year ended December 31, 2015.

As of December 31, 2015, the Company had unrecognized equity-based compensation expense related to the Common Shares transferred from the pool of Founder's Shares to employees and nonemployees with vesting restrictions of $0.1 million and $1.3 million, respectively. The total unrecognized compensation cost for the awards is adjusted for future forfeitures. The Company expects to recognize total unrecognized compensation cost over a remaining weighted-average period of 2.3 years. The fair value of nonemployee shares vested during the years ended December 31, 2014 and 2015, based on estimated fair values of the shares underlying the restricted share awards on the day of vesting, was $0.3 million and $0.6 million, respectively. The fair value of employee shares vested during the years ended December 31, 2014 and 2015, based on estimated fair values of the shares underlying the restricted share awards on the day of vesting, was $0 and $0.1 million, respectively.

TRACR Awards

Prior to the share exchange transaction with the Company in March 2015, upon approval of the TRACR Board of Directors, certain employee and non-employee advisors of TRACR were granted TRACR ordinary shares, restricted ordinary shares and certain subscription rights to ordinary shares of TRACR. These restricted shares were subject to certain transfer restrictions and repurchase rights.

The expense related to equity-based compensation awards granted to employees and non-employees advisors by the TRACR prior to the share exchange transaction was $0.2 million and $0.2 million, respectively, for the years ended December 31, 2014 and 2015.

In March 2015, pursuant to the share exchange transaction with the Company, holders of TRACR ordinary shares, restricted ordinary shares and certain subscription rights to ordinary shares were granted replacement awards of Common Shares, restricted share awards and subscription rights to Common Shares in exchange for TRACR ordinary shares held and subscription rights for TRACR shares. Pursuant to the share exchange transaction, the Company issued 255,854 Common Shares to the founders of TRACR, 196,809 restricted shares to employee and non-employee advisors, and 137,765 Common Shares to Fay Corp.

The Company recorded the incremental fair value associated with the fully vested portion of the replacement awards immediately upon issuance to the holder as this portion was attributable to services performed prior to the share exchange. The expense related to the fully vested portion of the replacement awards was $0.9 million for the year ended December 31, 2015. The Company recorded the fair value of the unvested portion of replacement awards of restricted share awards granted pursuant to the share exchange transaction over the associated service period as described in restricted stock awards above.

Fay Corp. Awards

In April 2014, in conjunction with the sale of its Series A-2 Preferred Shares, the founders and an investor transferred 357,780 Common Shares to Fay Corp. for the purpose of future issuances of equity-compensation awards to employees and nonemployee advisors. In March 2015, pursuant to the share exchange transaction between TRACR and the Company, the Company issued 137,765 Common Shares to Fay Corp. for certain TRACR subscription rights that were outstanding as of the exchange date. A summary of the status of and changes in Common Shares held by Fay Corp. as of December 31, 2014 and 2015 is as follows:

	Shares	Weighted-Average Grant Date Fair Value per Share
Common Shares outstanding held by Fay Corp. as of December 31, 2013	—	
Common Shares issued to Fay Corp.	357,780	
Common Shares outstanding held by Fay Corp. as of December 31, 2014	357,780	
Common Shares issued to Fay Corp.	137,765	
Common Shares transferred from Fay Corp.	(227,761)	$ 13.04
Common Shares outstanding held by Fay Corp. as of December 31, 2015	267,784	

During the year ended December 31, 2015, Fay Corp. transferred a total of 227,761 Common Shares, subject to certain vesting conditions, to three employees of the Company.

In September 2015, Fay Corp. transferred 135,000 Common Shares to one employee of the Company of which 120,000 Common Shares are subject to service-based vesting conditions and 15,000 Common Shares are subject to performance-based vesting conditions. Unvested Common Shares may be repurchased in certain circumstances from the holder upon termination of the holder's service relationship with the Company. Both vested and unvested shares are subject to repurchase at the original purchase price upon certain triggering events such as termination for cause, material breach of agreement and insolvency of the holder. At December 31, 2015, none of the 15,000 Common Shares with performance-based vesting conditions were vested, however, 4,500 Common Shares were deemed probable of vesting.

In September 2015, Fay Corp. transferred 92,761 Common Shares, of which 39,361 Common Shares were transferred pursuant to the TRACR share exchange transaction, to two employees of the Company. The Common Shares are subject to service-based vesting conditions and unvested Common Shares may be repurchased in certain circumstances from the holder upon termination of the holder's service relationship with the Company. Both vested and unvested shares are subject to repurchase at the original purchase price upon certain triggering events such as termination for cause, material breach of agreement and insolvency of the holder.

A summary of the status of and changes in vesting status of restricted shares transferred from Fay Corp. as of December 31, 2014 and 2015 is as follows:

	Shares	Weighted-Average Grant Date Fair Value per Share
Unvested Common Shares transferred from Fay Corp. as of December 31, 2014	—	—
Transferred	227,761	$ 13.04
Vested	(51,458)	$ 13.04
Unvested Common Shares transferred from Fay Corp. as of December 31, 2015	176,303	$ 13.04

The Company recorded equity-based compensation expense for the Common Shares issued with vesting restrictions from Fay Corp. to the three employees as the awards represented compensation for services to be performed for the benefit of the Company. As no Common Shares were transferred from Fay Corp. in 2014, there is no expense for the year ended December 31, 2014. The expense related to the Common Shares transferred from Fay Corp. to employees with vesting restrictions was $0.6 million for the year ended December 31, 2015.

As of December 31, 2015, the Company had unrecognized equity-based compensation expense related to the Common Shares transferred from Fay Corp. to employees with vesting restrictions of $1.8 million. The total unrecognized compensation cost for the awards are adjusted for future forfeitures. The Company expects to recognize total unrecognized compensation cost over a remaining weighted-average period of 3.0 years. The fair value of employee shares vested during the year ended December 31, 2015, based on estimated fair values of the shares underlying the restricted share awards on the day of vesting, was $0.7 million.

In March 2015, pursuant to the share exchange transaction with the Company, holders of certain subscription rights to ordinary shares of TRACR agreed to exchange these subscription rights for 137,765 Common Shares and restricted Common Shares of the Company to be issued from Fay Corp. following the share exchange. During the year ended December 31, 2015, Fay Corp. had transferred 39,361 Common Shares pursuant to the TRACR share exchange transaction to two employees. Pursuant to the share exchange transaction, Fay Corp. agreed to transfer 98,404 shares of fully vested Common Shares from Fay Corp. to two nonemployee directors. Accordingly, the Company recorded $0.2 million in equity compensation expense during the year ended December 31, 2015 relating to the subscription rights to Common Shares held by Fay Corp.

13. Income Taxes

The Company is subject to U.S. federal and various state corporate income taxes as well as taxes in foreign jurisdictions for the foreign parent and where foreign subsidiaries have been established. Loss before provision for income taxes and the provision for income taxes consist of the following (in thousands):

	Year Ended December 31,	
	2014	2015
Domestic	$ —	$ 593
Foreign	(6,863)	(26,414)
Total	$ (6,863)	$ (25,821)
The benefit from (provision for) for income taxes consists of:		
Current		
Federal	$ —	$ (23)
State	—	(12)
Foreign	(11)	(26)
Total Current	(11)	(61)
Deferred:		
Federal	—	(37)
State	—	65
Foreign	74	26
Total Deferred	74	54
Total	$ 63	$ (7)

A reconciliation of the federal statutory corporate income tax rate to the effective income tax rate for the years ended December 31, 2014 and 2015 is as follows:

	Year Ended December 31,	
	2014	2015
Income tax provision at federal statutory rate:	10.3%	10.3%
Increase (decrease) in tax resulting from:		
State Taxes	0.0%	0.1%
Nondeductible expenses	0.0%	0.0%
Foreign rate differential	1.8%	-1.4%
Stock-based compensation	-1.1%	-1.4%
Research credits	0.0%	0.6%
Valuation Allowance	-10.1%	-8.2%
Effective income tax rate	0.9%	0.0%

The federal statutory rate reflects the Switzerland mixed company service rate.

The components of deferred income taxes were as follows as of December 31 (in thousands):

	2014	2015
Deferred tax assets		
Accruals and reserves	$ 40	$ 189
Net operating loss carryforwards	1,396	2,600
Depreciation	1	—
Other deferred tax assets	3	72
Deferred revenue	—	406
Research credit	—	104
Less: valuation allowance	(1,370)	(2,892)
Deferred tax assets	70	479
Deferred tax liabilities		
Depreciation	—	(321)
Intangible assets	(95)	(80)
Other deferred tax liabilities	(4)	(53)
Deferred tax liabilities	(99)	(454)
Long term deferred taxes	$ (29)	$ 25

The Company has a valuation allowance in Switzerland and the UK for TRACR primarily related to net operating loss carryforwards. The Company believes these deferred tax assets do not meet a more likely than not criteria of being realized. Accordingly, the Company has a valuation against these deferred tax assets in these foreign jurisdictions. The valuation allowance increased by $1.5 million during 2015, which is primarily attributable to losses in Switzerland. The Company does not have a valuation allowance against the US deferred tax assets.

As of December 31, 2015, the Company had available foreign net operating loss carryforwards of $26.9 million which begin to expire in 2020. The Company has Federal and state research and development credit carryforwards of $0.1 million and $0.1 million, respectively. The Federal and state research credits begin to expire in 2035.

ASC 740 clarifies the accounting for uncertainty in income taxes recognized in an enterprise’s financial statements by prescribing a minimum recognition threshold and measurement of a tax position taken or expected to be taken in a tax return.

The aggregate changes in gross unrecognized tax benefits during the years ended December 31, 2014 and 2015 were as follows (in thousands):

	Year Ended December 31,	
	2014	2015
Balance at beginning of year	$ —	$ —
Increases for tax positions taken during current period	—	49
Increases for tax positions taken in prior periods	—	—
Increases for acquired tax positions taken in prior period	—	—
Decreases for acquired tax positions within measurement window	—	—
Decreases for tax positions taken in prior periods	—	—
Decreases for lapse in statutes	—	—
Balance at end of year	$ —	$ 49

As of December 31, 2014 and December 31, 2015, the Company had gross unrecognized tax benefits of $0.1 million of which the entire amount, if recognized, would favorably impact the effective tax rate. The Company classifies interest and penalties related to income taxes as a component of its provision for income taxes, and the amount of interest and penalties recorded as of December 31, 2014 and 2015 in the statements of operations and balance sheet was immaterial. The Company does not expect any material changes in the amounts of unrecognized tax benefits over the next 12 months.

The Company files income tax returns in the U.S. federal jurisdiction, Massachusetts, and foreign jurisdictions. The Company is subject to U.S federal, Massachusetts, and foreign income tax examinations by tax authorities for all years.

14. Net loss Per Share Attributable to Common Shareholders

As described in Note 2 the Company computes basic and diluted earnings (loss) per share using a methodology that gives effect to the impact of outstanding participating securities (the “two-class method”). As the years ended December 31, 2014 and 2015 resulted in net losses, there is no income allocation required under the two-class method or dilution attributed to weighted average shares outstanding in the calculation of diluted loss per share.

Basic and diluted net loss per common share are calculated as follows (in thousands, except share and per share data):

	Year Ended December 31,	
	2014	2015
Numerator:		
Net loss	$ (6,800)	$ (25,828)
Loss attributable to noncontrolling interest	536	325
Loss on extinguishment of redeemable convertible preferred shares	(745)	—
Net loss attributable to common stockholders—basic and diluted	$ (7,009)	$ (25,503)
Denominator:		
Weighted-average common shares used in net loss per share attributable to common stockholders—basic and diluted	1,068,000	1,511,225
Net loss per share attributable to common stockholders—basic and diluted	$ (6.56)	$ (16.88)

The following Common Share equivalents, presented on an as converted basis, were excluded from the calculation of net loss per share for the periods presented, due to their anti-dilutive effect (in thousands):

	Year Ended December 31,	
	2014	2015
Convertible preferred shares	1,068,000	5,651,105
Conversion of convertible notes	—	1,233,296
Dr. Emmanuelle Charpentier call option	—	98,405
Outstanding options	—	581,999
Unvested restricted shares	—	42,838
	1,068,000	7,607,643

15. Related Party Transactions

In connection with the Series A-3 Preferred Share financing, the Company paid $0.2 million on behalf of investors for legal and consulting costs incurred for the preparation and completion of the transaction.

The Company is a party to intellectual property license agreements with Dr. Emmanuelle Charpentier. In addition, Dr. Charpentier is a consultant to the Company and holds a 17.9% noncontrolling interest in TRACR. During the years ended December 31, 2014 and 2015, the Company paid Dr. Charpentier a total of $0.1 million and $34,000, respectively, in consulting, licensing and other fees. As of December 31, 2015, the Company owes Dr. Charpentier approximately $1.0 million of additional fees primarily related to the Vertex Collaboration Agreement.

Subsequent to the year ended December 31, 2015, the Company formed a joint venture with Bayer Healthcare LLC (“Bayer”). As a part of the agreement to form the joint venture, the Company also issued a convertible loan to Bayer, which then immediately converted in Series B Preferred Shares, see Note 16.

16. Subsequent Events

For the purposes of the financial statements as of December 31, 2014, December 31, 2015 and the periods and year then ended, the Company has evaluated the subsequent events through May 13, 2016, the date the audited financial statements were issued.

Joint Venture with Bayer Healthcare LLC

On December 19, 2015, the Company entered into an agreement to establish the Bayer Joint Venture with Bayer to discover, develop and commercialize new breakthrough therapeutics to cure blood disorders, blindness, and congenital heart disease. On February 12, 2016, the Company and Bayer completed the formation of the joint venture entity, Casebia Therapeutics LLP, a limited liability partnership formed in the United Kingdom. CRISPR contributed its proprietary CRISPR/Cas9 gene editing technology and intellectual property for selected disease indications and Bayer contributed its protein engineering expertise and relevant disease know-how.

Additionally, Bayer will provide up to $300 million to the joint venture over the next five years. The joint venture will pay the Company a technology access fee of $35 million in exchange for access to the Company’s intellectual property. In March 2016, the Company received $20 million of the technology access fee and will receive the remaining $15 million upon the satisfaction of certain conditions not yet realized.

Convertible Loan with Bayer Healthcare LLC

Concurrent with the execution of the Bayer Joint Venture agreement, the Company also entered into a Convertible Loan Agreement (“Bayer Convertible Loan”) with Bayer for $35 million. The Bayer Convertible Loan accrues interest at 2.0% per annum and matured on January 29, 2016 (the “Maturity Date”). On January 29, 2016, the Company issued the Bayer Convertible Loan in exchange for aggregate net proceeds of $35.0 million. The Bayer Convertible Loan included various embedded conversion, redemption and other features, none of which required separate accounting from the host instrument under ASC 815. Amounts recorded for issuance costs are being amortized to interest expense over the life of the loan. On January 29, 2016, simultaneously with the issuance of the loan, all of the outstanding principal plus accrued interest under the Convertible Loan was automatically converted into 781,599 Series B Preferred Shares.

Conversion of Convertible Loans to Series B Preferred Shares

On January 29, 2016, concurrent with the issuance of the Bayer Convertible Loan, all of the outstanding principal plus accrued interest under the $35.0 million Bayer Convertible Loan automatically converted into 781,599 Series B Preferred Shares at $44.78 per share. The receipt of $35.0 million in proceeds under the Bayer Convertible Loan in exchange for equity securities, combined with the $38.2 million in proceeds from Vertex Convertible Loan, triggered an automatic conversion provision of the Vertex Convertible Loan Agreement. Accordingly, on January 29, 2016, the Vertex Convertible Loan, including loans from existing shareholders, also converted into 857,783 of Series B Preferred Shares at $44.78 per share.

Subscription Agreement with Bayer Global Investments B.V.

In December 2015, the Company entered into a Subscription Agreement, with Bayer BV. Pursuant to the Subscription Agreement, Bayer BV was given the option, at its election, to purchase up to $35.0 million of the Company's Common Shares in a private placement concurrent with the Company's IPO at a per share price equal to the public offering price of this offering. In April 2016, Bayer BV provided the Company with written notice of its exercise of the option. The Company may reduce the amount of Bayer BV's purchase under the Subscription Agreement at its sole discretion, subject to the terms of the Subscription Agreement.

Series A-3 Preferred Shares Subscription Receivable

On May 5, 2016, the balance of the Series A-3 Preferred Share subscription receivable of $7.08 per share, or $22.8 million, was called by the Board of Directors. The Series A-3 Preferred Shares are automatically converted to Common Shares at a rate of ten Series A-3 Preferred Shares for each Common Share if the payment of the Series A-3 Preferred Shares subscription receivable is not made on or before June 17, 2016.

Operating Leases

Subsequent to December 31, 2015, the Company entered into two sublease agreements for office and laboratory space. The first of these begins on April 1, 2016, and expires on January 31, 2017, and shall continue on a tenancy-at-will basis with either party having the right to terminate with thirty days of notice. The Company's contractual obligation related to lease payments over the term of this sublease is approximately $0.3 million.

The second lease is expected to begin on February 1, 2017, and expires ten years from the commencement date. The Company has the option to extend the term of the lease by five years. The Company's contractual obligation related to lease payments over the term of the sublease is approximately $56.2 million.

Shares

CRISPR Therapeutics AG

Common Shares

PRELIMINARY PROSPECTUS

, 2016

Citigroup
Piper Jaffray
Barclays
Guggenheim Securities

Until , 2016 (25 days after the date of this prospectus), all dealers that buy, sell or trade our common shares, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealer's obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

PART II
INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution

The following table sets forth the costs and expenses, other than the underwriting discounts and commissions, payable by the registrant in connection with the sale of common shares being registered. All amounts are estimates except for the Securities and Exchange Commission, or SEC, registration fee, the Financial Industry Regulatory Authority, or FINRA, filing fee and the NASDAQ Global Market, or NASDAQ, listing fee:

Expenses	Amount
U.S. Securities and Exchange Commission registration fee	$ *
NASDAQ Global Market listing fee	125,000
FINRA filing fee	*
Printing and engraving expenses	*
Legal fees and expenses	*
Accounting fees and expenses	*
Transfer agent fees and expenses	*
Miscellaneous costs	*
Total	$ *

* To be provided by amendment.

All amounts in the table are estimates except the U.S. Securities and Exchange Commission registration fee, the NASDAQ listing fee and the FINRA filing fee. The Company will pay all of the expenses of this offering.

Item 14. Indemnification of Directors and Officers

Under Swiss law, a corporation may indemnify its directors or officers against losses and expenses (except for such losses and expenses arising from willful misconduct or negligence, although legal scholars advocate that at least gross negligence be required), including attorney's fees, judgments, fines and settlement amounts actually and reasonably incurred in a civil or criminal action, suit or proceeding by reason of having been the representative of, or serving at the request of, the corporation.

Subject to Swiss law, Article 29 of our articles of association provides for indemnification of the existing and former members of our board of directors, executive management, and their heirs, executors and administrators, against liabilities arising in connection with the performance of their duties in such capacity, and permits us to advance the expenses of defending any act, suit or proceeding to members of our board of directors and executive management.

In addition, under general principles of Swiss employment law, an employer may be required to indemnify an employee against losses and expenses incurred by such employee in the proper execution of their duties under the employment agreement with the company.

We intend to enter into indemnification agreements with each of the members of our board of directors and executive officers in the form to be filed as an exhibit to this Registration Statement upon the closing of this offering.

In the underwriting agreement that we enter into in connection with the sale of the common shares being registered hereby, a form of which will be filed as Exhibit 1.1 to this Registration Statement, the underwriters will agree to indemnify, under certain conditions, us, our directors, our officers and persons who control us within the meaning of the Securities Act of 1933, as amended, the Securities Act, against certain liabilities.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Company, the Company has been advised that, in the opinion of the U.S. Securities and Exchange Commission, such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable.

Item 15. Recent Sales of Unregistered Securities

The following sets forth information regarding all unregistered securities sold during the last three fiscal years. Within the last three years, the registrant has issued and sold the following securities:

1. Since October 31, 2013, the registrant issued and sold 967,500 common shares for aggregate consideration of CHF 106,800.
2. On November 5, 2013, the registrant issued and sold 132,000 of its Series A-1 Preferred Shares for aggregate consideration of approximately CHF 501,600.
3. On May 6, 2014, the registrant issued and sold 936,000 of its Series A-2 Preferred Shares for aggregate consideration of approximately CHF 9.5 million.
4. On April 14, 2015, the registrant issued and sold 3,227,401 of its Series A-3 Preferred Shares for aggregate consideration of approximately $45.7 million.
5. On March 24, 2015, the registrant issued 590,428 common shares in exchange for 4,600 ordinary shares of TRACR Hematology Limited and the assignment of certain rights to subscribe for ordinary shares of TRACR Hematology Limited.
6. On May 4, 2015, the registrant issued and sold 1,355,704 of its Series B Preferred Shares for aggregate consideration of approximately CHF 28.0 million.
7. On January 29, 2016, the registrant issued 1,639,382 of its Series B Preferred Shares in connection with the conversion of outstanding convertible notes with aggregate principal and accrued interestof approximately $73.4 million.
8. Since April 15, the registrant issued options to purchase 581,999 shares of its common shares to its employees with an exercise price of 10.44 per share.

We deemed the offers, sales and issuances of the securities described in paragraphs (1) through (7) above to be exempt from registration under the Securities Act, in reliance on Section 4(a)(2) of the Securities Act, regarding transactions by an issuer not involving a public offering. All purchasers of securities in transactions exempt from registration pursuant to Section 4(a)(2) represented to us that they were acquiring the shares for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time. The purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration statement or an available exemption from such registration.

We deemed the issuances of our common stock and options to purchase common stock in paragraph (8) to be exempt from registration under the Securities Act either in reliance on Rule 701 of the Securities Act as offers and sales of securities under compensatory benefit plans and contracts relating to compensation in compliance with Rule 701, or in reliance on Section 4(a)(2), as transactions by an issuer not involving a public offering. Each of the recipients of securities in any transaction exempt from registration either received or had adequate access, through employment, business or other relationships, to information about us.

There were no underwritten offerings employed in connection with any of the transactions set forth above.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits. See the Exhibit Index attached to this Registration Statement, which is incorporated by reference herein.

(b) Financial Statement Schedules. Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

Item 17. Undertakings.

The undersigned Registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question of whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

1. For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this Registration Statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this Registration Statement as of the time it was declared effective.
2. For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-1 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Basel, Switzerland on , 2016.

CRISPR THERAPEUTICS AG

By: _____

Name: Dr. Rodger Novak
Title: Chief Executive Officer

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Dr. Rodger Novak and Marc A. Becker and each of them, individually, as his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place and stead in any and all capacities, in connection with this registration statement, including to sign in the name and on behalf of the undersigned, this registration statement and any and all amendments thereto, including post-effective amendments and registrations filed pursuant to Rule 462 under the U.S. Securities Act of 1933, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the U.S. Securities and Exchange Commission, granting unto such attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or his substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed by the following persons on the date indicated below in the capacities indicated:

Signature	Title	Date
Dr. Rodger Novak	Chief Executive Officer (principal executive officer)	, 2016
Marc A. Becker	Chief Financial Officer (principal financial officer and principal accounting officer)	, 2016
Dr. N. Anthony Coles	Chairman and Director	, 2016
Dr. Ali Behbahani	Director	, 2016
Dr. Bradley Bolzon	Director	, 2016
Dr. Simeon J. George	Director	, 2016
Kurt von Emster	Director	, 2016
Dr. Thomas Woiwode	Director	, 2016
Dr. Pablo Cagnoni	Director	, 2016
Marc A. Becker	Authorized Representative in the United States	, 2016

EXHIBIT INDEX

The following documents are filed as part of this registration statement:

1.1*	Form of Underwriting Agreement
3.1*	Form of Articles of Association
4.1*	Subscription Agreement, dated December 19, 2015, by and between CRISPR Therapeutics AG and Bayer Global Investments B.V.
5.1*	Opinion of Vischer AG, Swiss counsel of CRISPR Therapeutics AG, as to the validity of the common shares
8.1*	Opinion of Vischer AG, Swiss counsel of CRISPR Therapeutics AG, as to Swiss tax matters
10.1*†	Joint Venture Agreement, dated December 19, 2015, between CRISPR Therapeutics AG and Bayer Healthcare LLC
10.2*†	Strategic Collaboration, Option and License Agreement, dated October 26, 2015, by and among CRISPR Therapeutics AG, CRISPR Therapeutics Limited, CRISPR Therapeutics, Inc., TRACR Hematology Ltd., Vertex Pharmaceuticals, Incorporated and Vertex Pharmaceuticals (Europe) Limited
10.3*†	License Agreement, dated April 15, 2014, by and between CRISPR Therapeutics AG and Emmanuelle Marie Charpentier
10.4*†	Patent Assignment Agreement, dated November 7, 2014, by and between CRISPR Therapeutics AG, Emmanuelle Marie Charpentier, the University of Vienna and Ines Fonfara
10.5*†	License Agreement, dated April 14, 2015, by and between TRACR Hematology Limited and Emmanuelle Marie Charpentier
10.6*	Form of Indemnification Agreement
10.7*	Shareholders' Agreement, dated April 13, 2015, by and among CRISPR Therapeutics AG and certain shareholders
10.8*	Employment Agreement, dated November 11, 2013, by and between Inception Genomics AG and Rodger Novak
10.9*	Employment Agreement, dated January 18, 2016, by and between CRISPR Therapeutics, Inc. and Marc A. Becker
10.10*	Offer Letter, dated July 10, 2015, by and between CRISPR Therapeutics, Inc. and Samarth Kulkarni
10.11*	Employment Agreement, dated February 18, 2015, by and between CRISPR Therapeutics, Inc. and Sven Ante Lundberg
10.12*	CRISPR Therapeutics AG 2015 Stock Option and Grant Plan
10.13*	CRISPR Therapeutics AG 2016 Stock Option and Incentive Plan
10.14*	IP Contribution Agreement, dated March 15, 2016, by and between CRISPR Therapeutics AG, Bayer HealthCare LLC and Casebia Therapeutics LLP
10.15*	Option Agreement, dated March 31, 2016, by and between CRISPR Therapeutics AG, Bayer HealthCare LLC and Casebia Therapeutics LLP
21.1*	Subsidiaries of the Registrant

23.1*	Consent of Ernst & Young LLP
23.2*	Consent of Vischer AG, Swiss counsel of CRISPR Therapeutics AG (included in Exhibit 5.1)
23.3*	Consent of Vischer AG, Swiss counsel of CRISPR Therapeutics AG (included in Exhibit 8.1)
23.4*	Consent of Goodwin Procter LLP (included in Exhibit 8.2)
24.1*	Powers of attorney (included on signature page to the registration statement)

* To be filed by amendment

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and this exhibit has been filed separately with the SEC.