CRISPR Therapeutics

Creating transformative gene-based medicines for serious diseases

Corporate Overview

November 2017

Forward-Looking Statements

This presentation and other related materials contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the timing of filing of clinical trial applications and INDs and timing of commencement of clinical trials, the timing, therapeutic value, development, and commercial potential of CRISPR/Cas-9 gene editing technologies and therapies, the sufficiency of CRISPR's cash resources and the intellectual property coverage and positions of CRISPR, its licensors and third parties. All statements, other than statements of historical facts, included or incorporated by reference in this presentation and other related materials, including statements regarding CRISPR's strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, and objectives of management, are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "target," "should," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. CRISPR may not actually achieve the plans, intentions, or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various factors, including: uncertainties regarding the intellectual property protection for CRISPR's technology and intellectual property belonging to third parties; uncertainties inherent in the initiation and completion of preclinical studies for CRISPR's product candidates; availability and timing of results from preclinical studies; whether results from a preclinical trial will be predictive of future results of the future trials; expectations for regulatory approvals to conduct trials or to market products; and those risks and uncertainties described under the heading "Risk Factors" in CRISPR's most recent annual report on Form 10-K, and in other filings that CRISPR has made or may make with the U.S. Securities and Exchange Commission.

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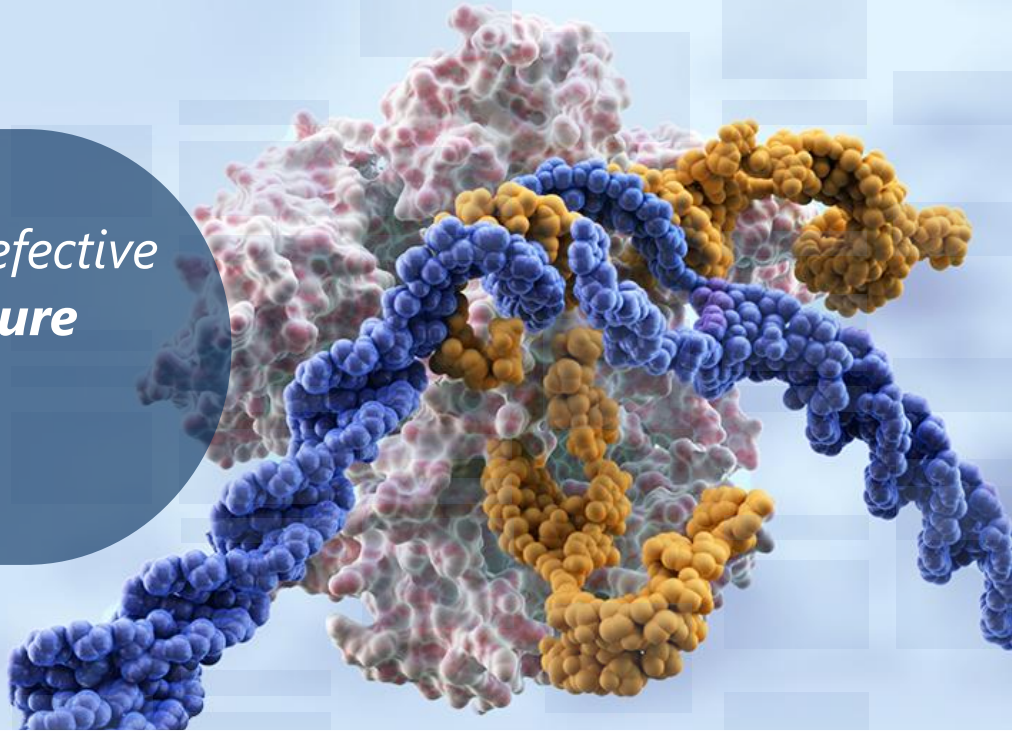
The CRISPR/Cas9 Revolution

> *A new technology for 'editing' defective genes has raised hopes for a* ***future generation of medicines***

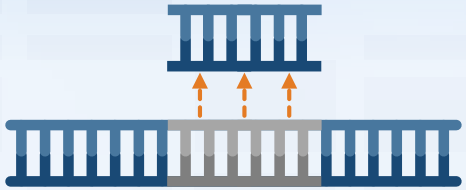
THE WALL STREET JOURNAL.



Specific, efficient, and versatile platform

DISRUPTION

DELETION



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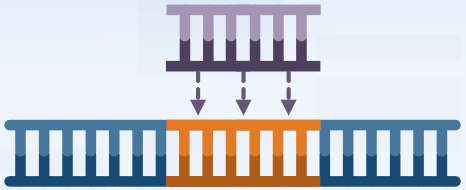


CRISPR Therapeutics Highlights

LEADING GENE-EDITING COMPANY	Rapidly translating revolutionary CRISPR/Cas9 technology into transformative therapies
PIONEERING CRISPR IN THE CLINIC	Lead program in hemoglobinopathies on track to enter clinical trials in 2018
NEXT-GENERATION I/O PLATFORM	Advancing wholly owned, potentially best-in-class gene-edited allogeneic CAR-T products toward the clinic
ADVANCING *IN VIVO* APPLICATIONS	Pursuing select *in vivo* indications enabled by in-licensed technologies, platform improvement, and strategic partners
UNIQUE CASEBIA JOINT VENTURE	50% ownership of Casebia broadens our pipeline and supports our platform improvement efforts; funded by ~$265M from Bayer
STRONG IP & FINANCIAL POSITION	Strong IP position, experienced leadership, 100+ people, >$250M current cash position

Our Portfolio

Program	Editing approach	Research	IND-enabling	Ph I/II	Partner	Structure
***Ex vivo:* Hematopoietic**						
CTX001: β-thalassemia	Disruption			*CTA filing end of 2017*	VERTEX	Collaboration
CTX001: Sickle cell disease (SCD)	Disruption			*IND filing 1H 2018*	VERTEX	Collaboration
Hurler syndrome (MPS-1)	Correction					Wholly-owned
Severe combined immunodeficiency (SCID)	Correction				CASEBIA	Joint venture
***Ex vivo:* Immuno-oncology**						
CTX101: CD19-positive malignancies	Various			*IND filing end of 2018*		Wholly-owned
Anti-BCMA Allogeneic CAR-T	Various					Wholly-owned
Anti-CD70 Allogeneic CAR-T	Various					Wholly-owned
***In vivo:* Liver**						
Glycogen storage disease Ia (GSD Ia)	Correction					Wholly-owned
Hemophilia	Correction				CASEBIA	Joint venture
***In vivo:* Other organs**						
Duchenne muscular dystrophy (DMD)	Disruption					Wholly-owned
Cystic fibrosis (CF)	Correction				VERTEX	License option

Our Therapeutic Programs

Hemoglobinopathies
Ex vivo *lead candidate in genetically-defined disease*

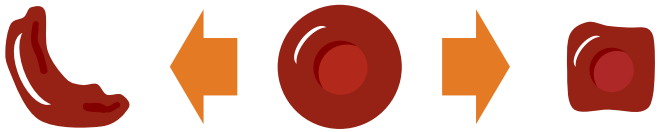
Immuno-oncology
Expand cell therapy platform with allo CAR-T pipeline

In vivo
Enable in vivo *applications through platform advancements*

Hemoglobinopathies – Devastating Blood Diseases

SICKLE CELL DISEASE (SCD) AND β-THALASSEMIA

Blood disorders caused by *mutations* in the β-globin gene



Sickle Cell | Normal Cell | **β-thalassemia**

Significant worldwide burden

300,000

60,000

Annual births in SCD and β-thalassemia, respectively

High morbidity and mortality

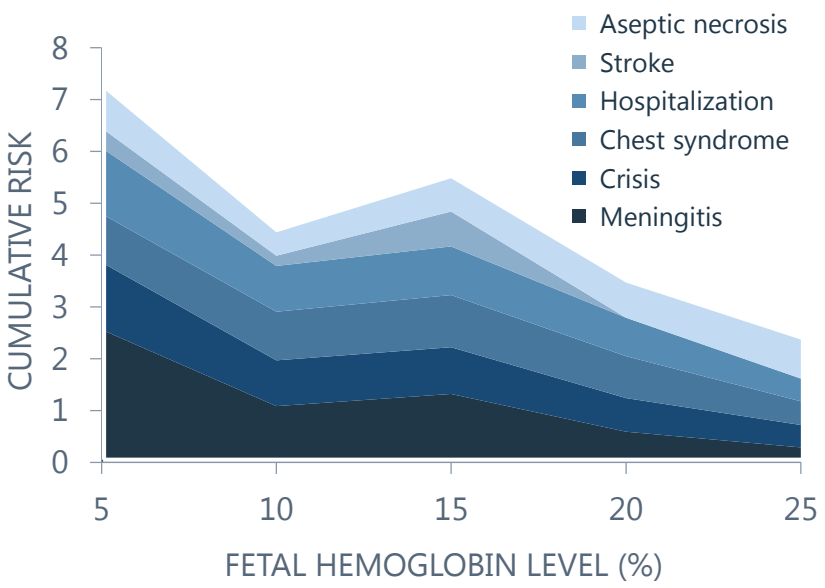
Anemia | Pain | **Early death**

Heavy burden of patient care

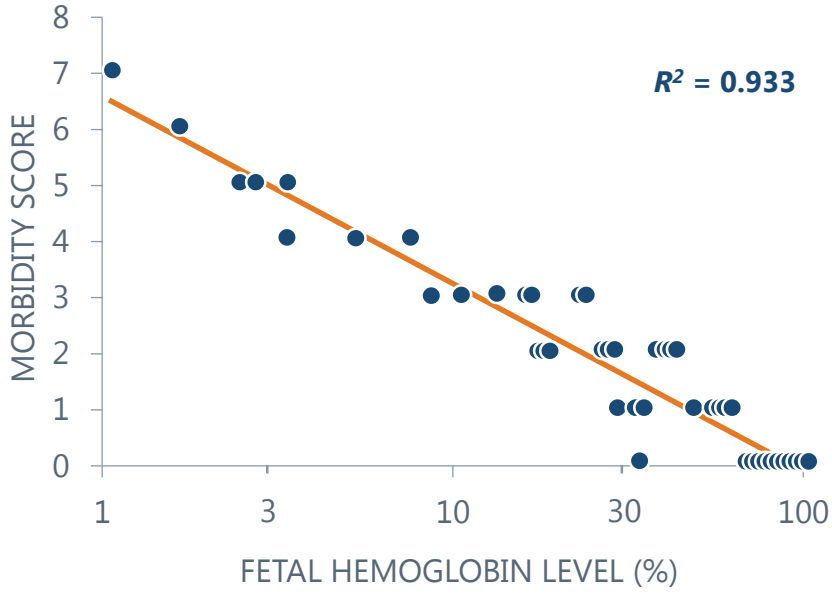
Frequent transfusions & hospitalizations

Our Approach – Upregulating Fetal Hemoglobin

REDUCED RISK OF EVENTS IN SICKLE CELL DISEASE[1]



REDUCED SYMPTOMS IN β-THALASSEMIA[2]



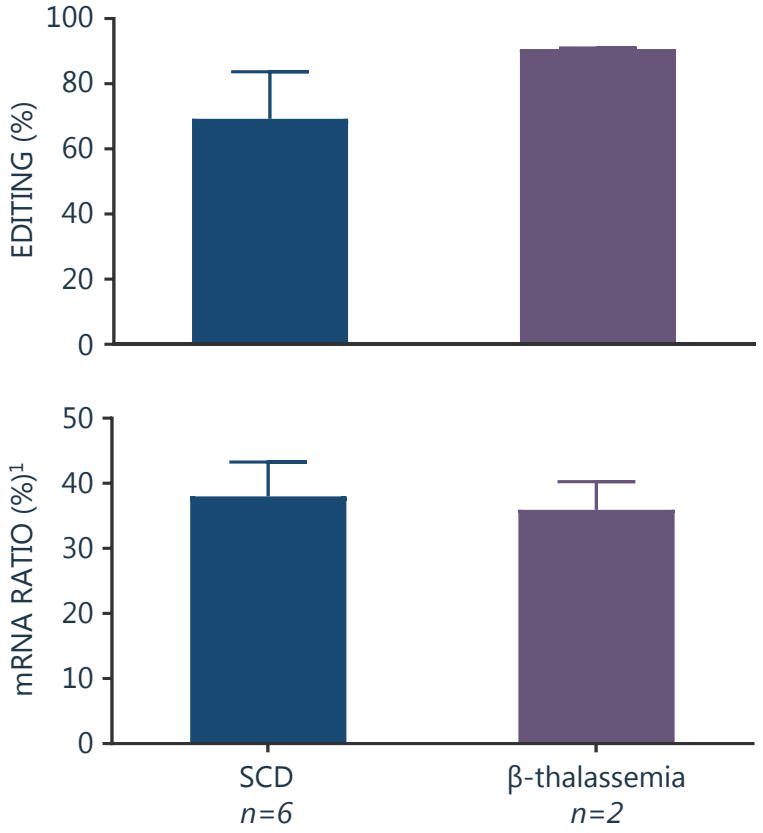
- **Naturally occurring genetic variants** cause **hereditary persistence of fetal hemoglobin** (HPFH), and **lead to reduced symptoms** in patients with sickle cell disease and β-thalassemia
- Our gene editing strategy aims to **recreate these variants** in symptomatic patients — an approach **supported by well-understood genetics**

1. Powars, *et al.* Blood 1984; 2. Musallam, *et al.* Blood 2012

CTX001 Leads to Upregulation of Fetal Hemoglobin

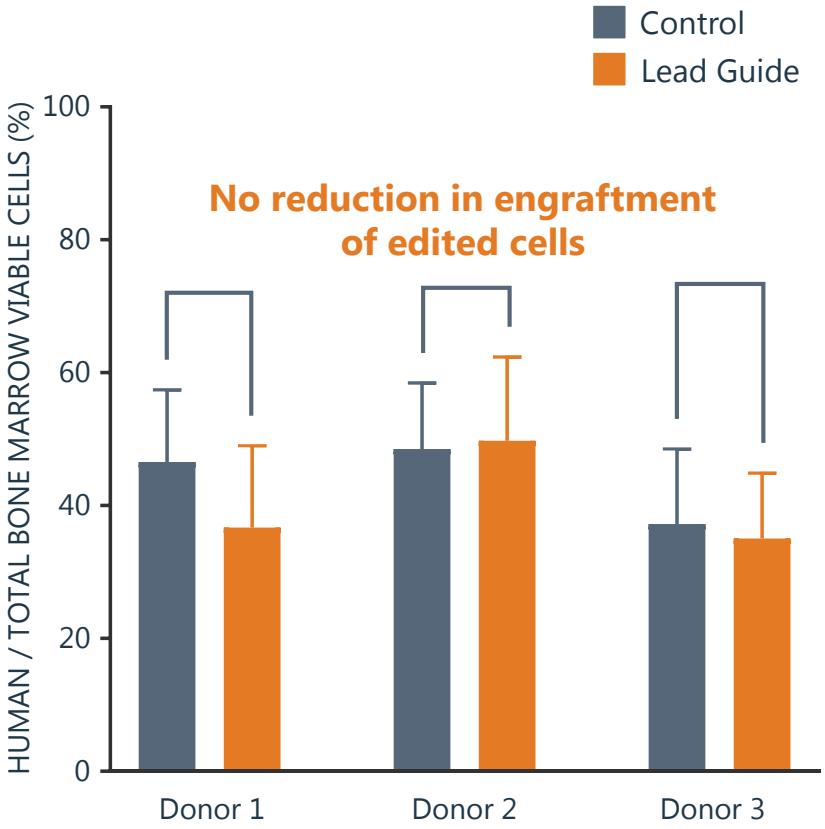
EDITING RESULTS IN HbF UPREGULATION

In vitro *editing efficiencies and globin mRNA ratios for lead guide*



CTX001 ENGRAFTS *IN VIVO* IN MICE

Bone marrow chimerism at 16 weeks



1. γ/(γ+β) for SCD and γ/α for β-thalassemia; background subtracted

On Track to File CTA for β-thalassemia by End of 2017

2015-2016	2017	2018-2019
***In Vitro* Proof-of-Concept and *In Vivo* Engraftment Studies** › Desired gene edits made with high efficiency and no detectable off-target cutting › Edits cause healthy and patient-derived cells to produce HbF › Edited cells engraft and persist in a mouse model	**GLP/Tox Studies** › Edited cells do not cause any adverse effects › No toxicity or tumorigenicity observed	**CTA[1] filing for β-thalassemia, with SCD to follow in 1H18** **Clinical Studies** › Demonstrate initial POC › Potential to expand into a registrational trial – pursuing accelerated path to approval
Process development for GMP manufacturing › Human CD34⁺ cells, Cas9 and guide RNAs		

1. Clinical Trial Application

Completed

Pioneering CRISPR Clinical Trial

CTX001-111

A single arm Phase 1/2 study to assess the safety and efficacy of CTX001 in patients with β-thalassemia

Patients

Up to 30 adult transfusion-dependent patients

Sites

Sites with extensive transplant experience in E.U. countries with significant disease burden

Endpoints

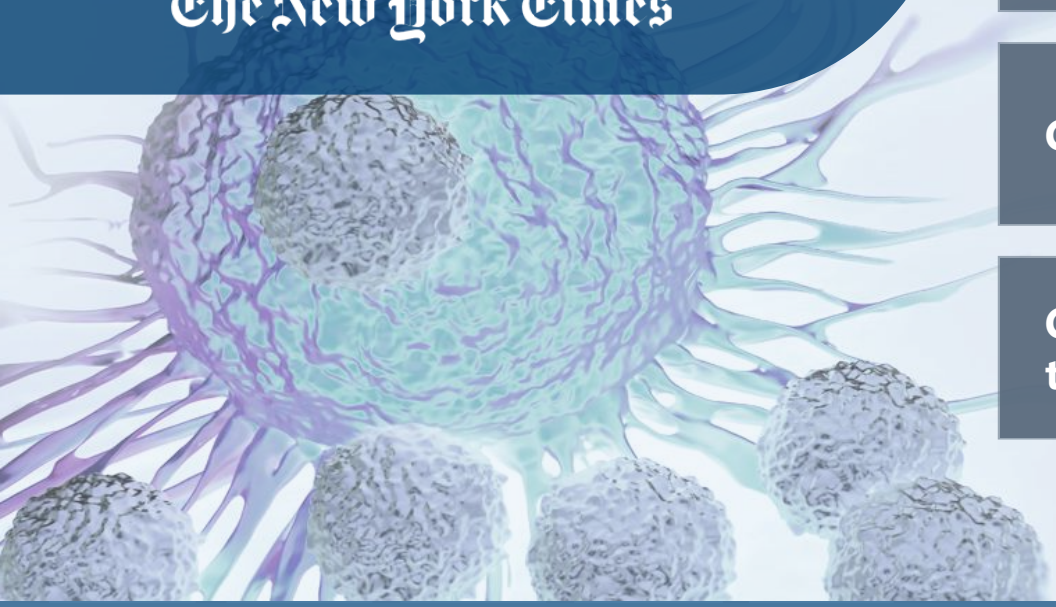
HbF levels and transfusion requirements are clinically relevant and easily measurable

Potential to expand into a registrational trial, as well as to additional genotype and age cohorts, if supported by safety and efficacy

Autologous CAR-T is Transformative, but has Limitations

CAR-T has generated **tremendous excitement . . .**

> *The first-ever treatment that genetically alters a patient's own cells to fight cancer, a milestone that is **expected to transform treatment in the coming years***
>
> The New York Times

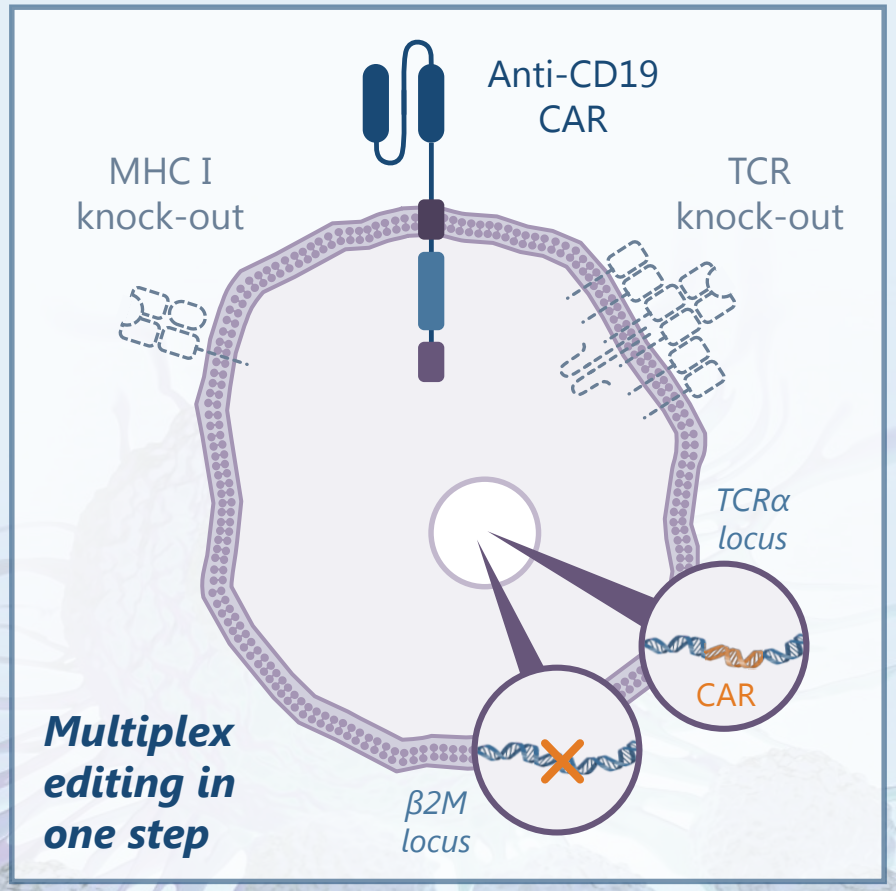


. . . But there are still **significant limitations** to autologous CAR-T

- **Patients progress or die while waiting**
- **Patient-to-patient variability**
- **Costly, complicated manufacturing**
- **Commercial challenges of bespoke therapy**

Our Approach: Gene-Edited Allogeneic CD19 CAR-T

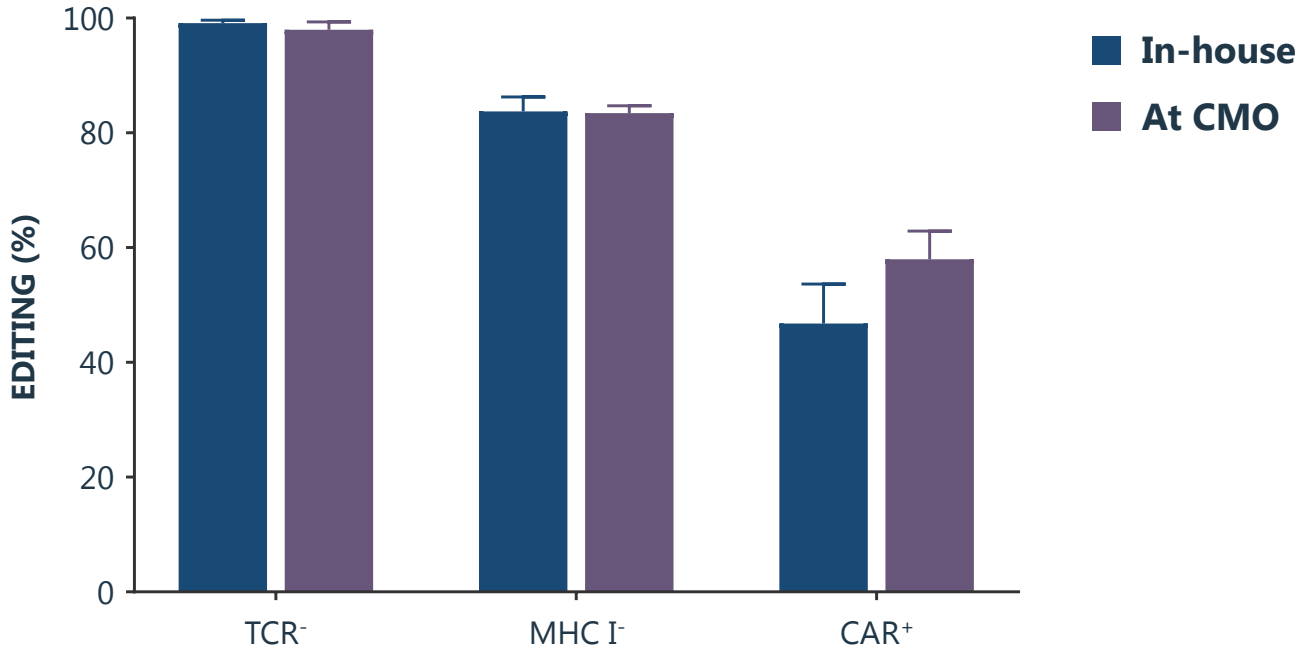
CTX101 – our initial immuno-oncology product candidate



CRISPR enables an allogeneic approach that **remedies issues with autologous CAR-T**

- **Product available immediately**
- **Consistent healthy-donor lymphocytes**
- **Low COGs and simpler manufacturing**
- **Off-the-shelf product – broader access**

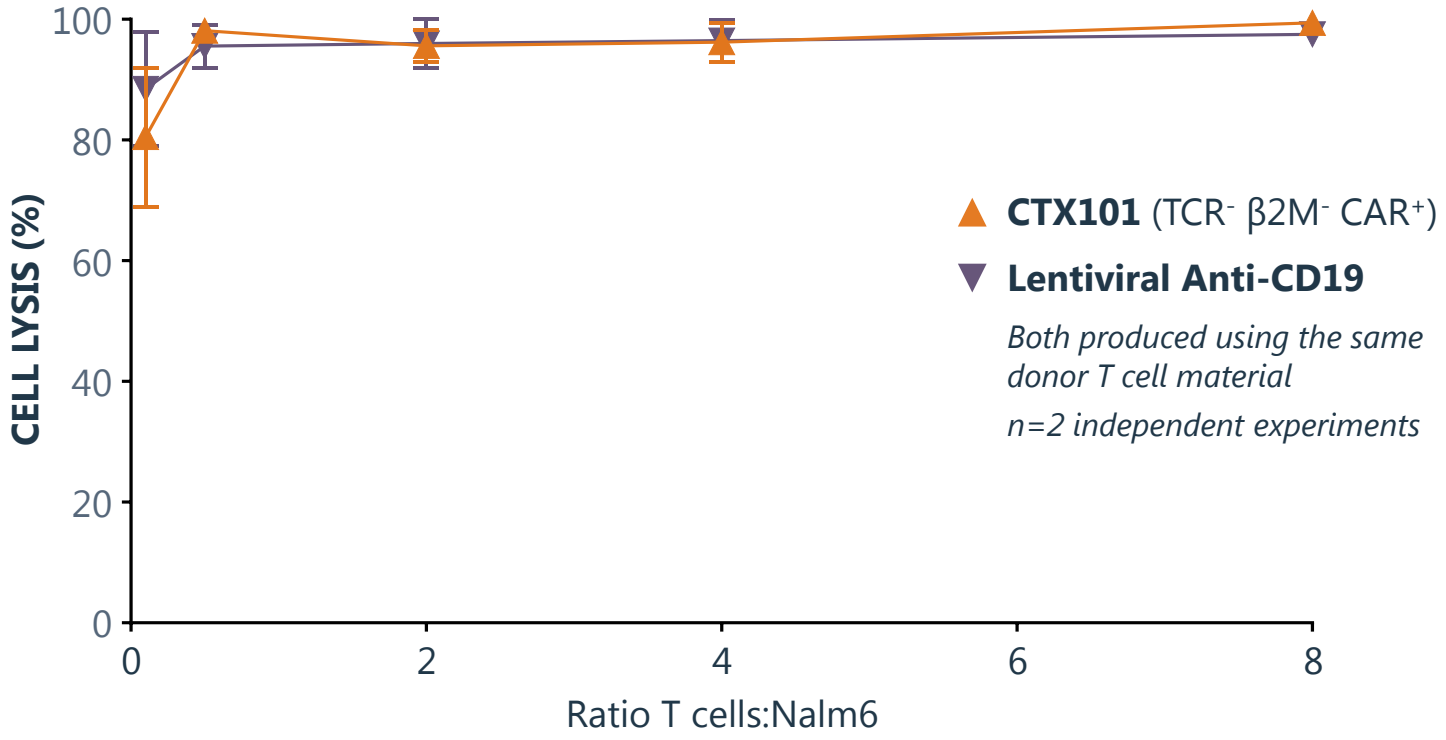
Equal or Better Editing Rates Achieved After Tech Transfer



Process development and manufacturing initiated for CTX101 – commencing IND-enabling studies

CTX101 Eliminates CD19-Expressing Tumor Cells *In Vitro*

CTX101 COMPARES FAVORABLY TO LENTIVIRAL "AUTOLOGOUS" CAR-T



Numerous Opportunities Beyond CTX101

Make rapid entry using validated tumor targets

Healthy-donor allo approach in well-validated tumor targets

CD19, BCMA

Expand into solid with novel targets and advanced editing

Precise edits to make CAR-T effective in solid tumors

CD70, resistance to tumor microenvironment

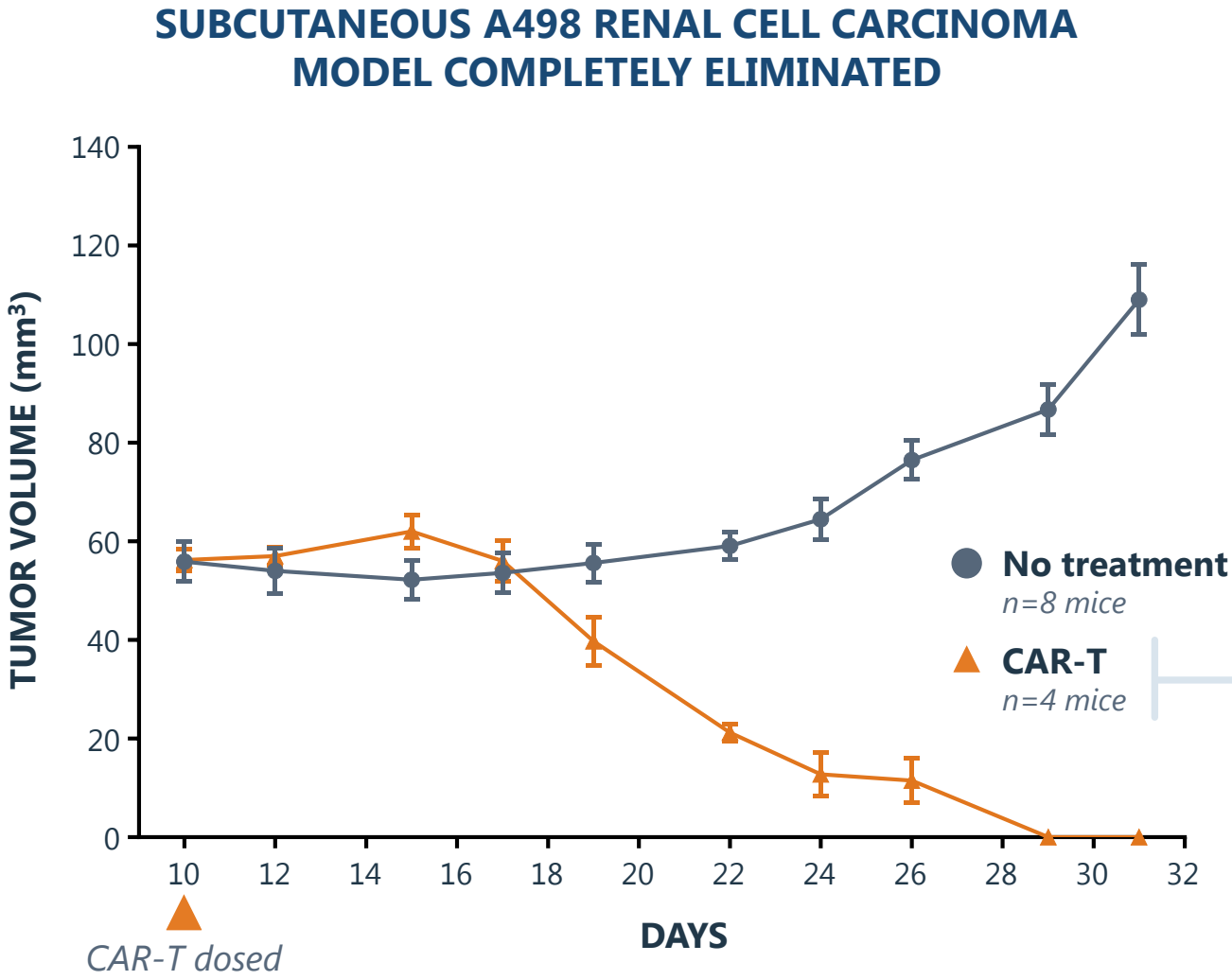
Unlock the full potential of CRISPR

Multiplex editing to enable more complex products

Switches, neoantigens, bispecifics

Collaborations with Neon and MGH to identify and exploit new targets

Gene-Edited Allo CAR-T Targeting CD70



- **>85% CAR⁺** using a proprietary single chain made in-house
- **>99% TCR knock-out** even before purification

Delivering CRISPR/Cas9 to Unlock *In Vivo* Applications

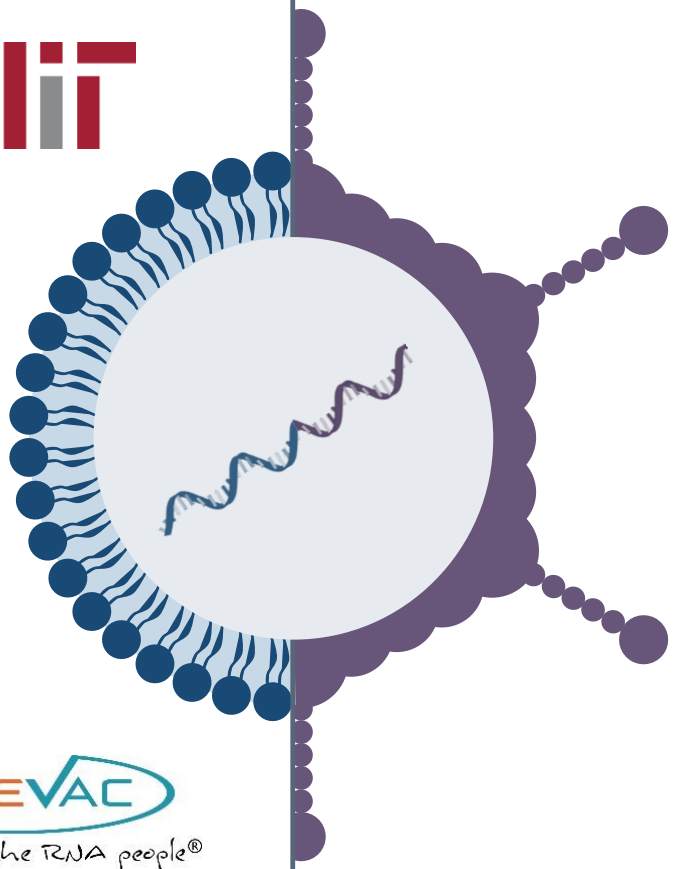
NON-VIRAL

Lipid Nanoparticles (LNPs)

- Increased potency
- Expansion beyond liver delivery
- Improved tolerability

Messenger RNA (mRNA)

- Controlled duration of expression
- Tissue specificity
- Increased potency



VIRAL

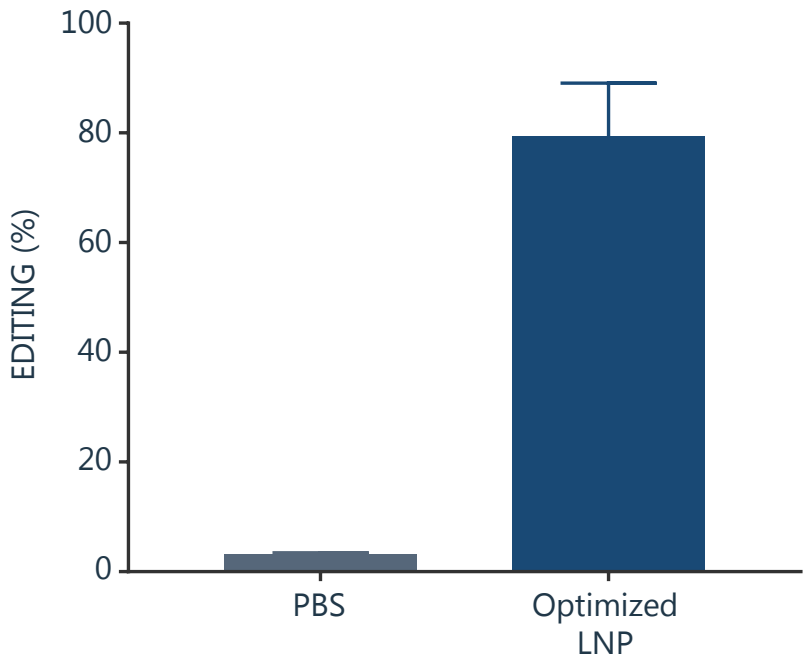
Adeno-Associated Virus (AAV)

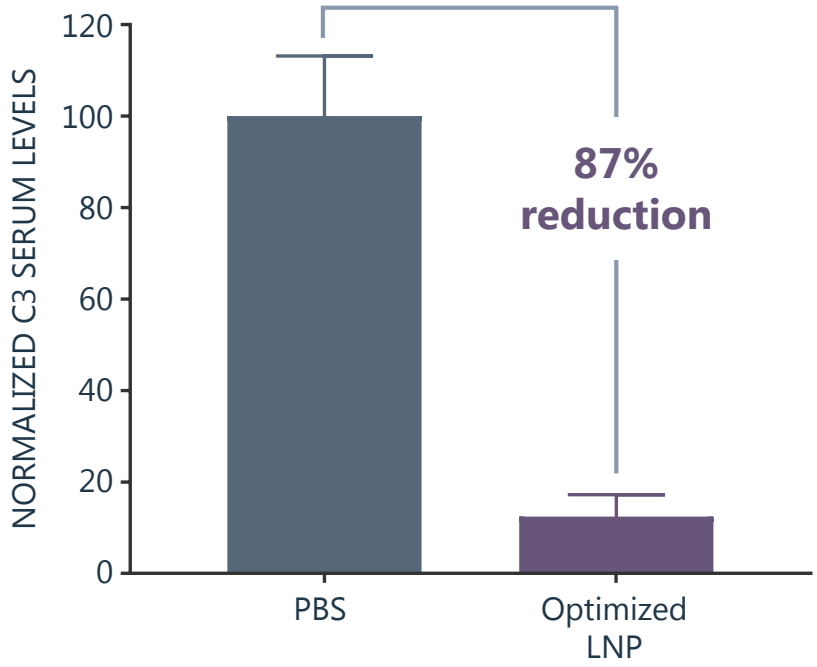
- Improved tissue specificity
- Reduced immunogenicity
- Self-inactivation

Potent Liver Editing Using Proprietary LNP Technology

SIGNIFICANT DECREASE IN SERUM C3 LEVELS AFTER EDITING *IN VIVO*

Editing and serum protein quantified in five mice following intravenous LNP dose





~80% editing in mouse livers and 87% reduction in serum C3 protein using just 1 mg/kg total RNA: ~3X higher potency than other published data

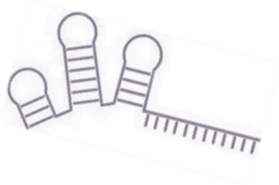
Optimizing the CRISPR/Cas9 Platform

NUCLEASE ENGINEERING

Enhance CRISPR/Cas9 system through protein engineering

GUIDE RNA OPTIMIZATION

Identify optimal guide RNA formats and sequences for therapeutic editing



PLATFORM ENHANCEMENT

ADVANCED EDITING

Improve efficiency of gene correction and multiplexing

STEM CELL ENGINEERING

Expand applications of gene-edited stem cells to treat disease

Fifty-Percent Ownership of Casebia Therapeutics

Committed IP
for select indications

Committed $370M
$265M to Casebia and $105M to CRISPR

THERAPEUTIC FOCUS AREAS

Hematology

Cardiology

Ophthalmology

Joint research on platform technology – protein engineering, delivery, etc.

CRISPR has full access at no cost to *all new* IP for use within the field of human therapeutics

Foundational Intellectual Property Landscape

	Foundational IP estate		Broad IP estate
Patent Filings	**EMMANUELLE CHARPENTIER**	**UC BERKELEY / U. VIENNA**	**BROAD INSTITUTE**
Human Therapeutics Licensees	CRISPR THERAPEUTICS	Intellia THERAPEUTICS via CARIBOU BIOSCIENCES	editas MEDICINE
Strategic Investors	Celgene, gsk		
Partners & Total Deal Size	BAYER, VERTEX, >$3B	NOVARTIS, REGENERON, >$3B	JUNO THERAPEUTICS, Allergan, <$2B

- Direct license to foundational IP covering all human therapeutic fields; term through 2033
- Four large pharma partnerships indicate strength of the Charpentier / Berkeley foundational IP estate
- Access to Vilnius IP estate through invention management agreement

Strong US and Global Foundational IP Position

UNITED STATES
First-to-invent

UC-CRISPR appealing interference decision in Federal Appeals Court

- Appeal ongoing to overturn Feb 2017 PTAB decision to end the first interference on technical grounds

Next steps

- Appeal expected to take ~12 months
- Multiple patent applications moving forward in parallel – both narrow and broad claims

EUROPE AND GLOBAL
First-to-file

UC-CRISPR granted foundational patents, including use in eukaryotes

- 3 patents granted between E.U. and U.K. include single-guide RNA & uses in all settings
- Patents of broad scope granted in China, Australia, New Zealand, Singapore, Mexico

Next steps

- Advancing applications globally in ~80 jurisdictions worldwide based on arguments developed in Europe

Experienced Management Team

RODGER NOVAK, MD
Chief Executive Officer & Director
Head of Anti-Infectives R&D, Sanofi

SAM KULKARNI, PHD
President & CBO; CEO-designate
Partner, McKinsey & Company

TONY HO, MD
Head of Research & Development
Head of Oncology Innovation, AstraZeneca

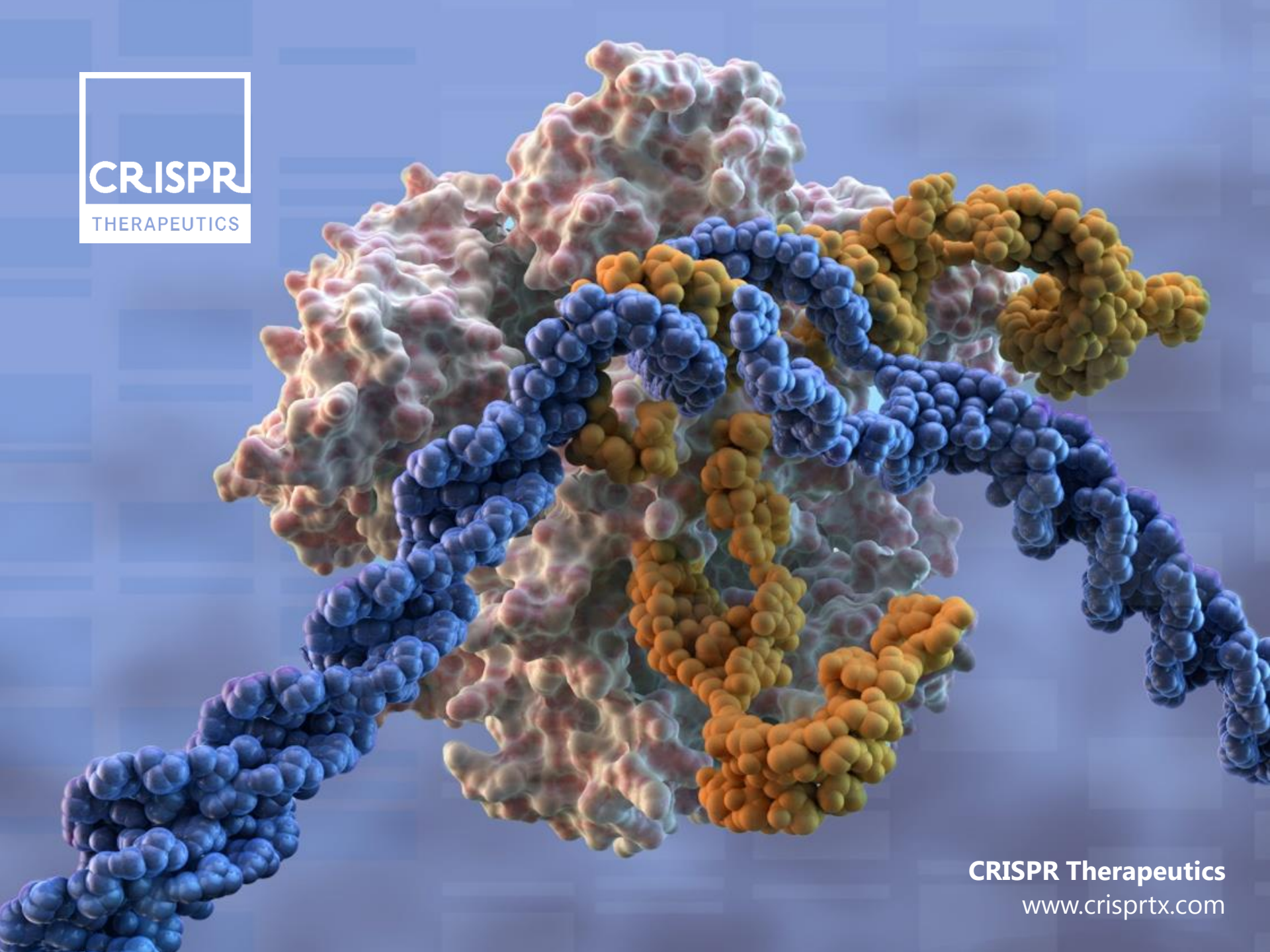
BILL LUNDBERG, MD
Chief Scientific Officer
Head of Translational Medicine, Alexion

MIKE TOMSICEK, MBA
Chief Financial Officer
Chief Financial Officer, Abiomed

KALA SUBRAMANIAN, PHD
SVP, Strategic Development & Operations
Global Head of Program Management, Novartis

TYLER DYLAN-HYDE, PHD
Chief Legal Officer
Partner, Morrison & Foerster

JIM KASINGER, JD
General Counsel & Corporate Secretary
General Counsel, Moderna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