UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-Q

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended March 31, 2022

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _____ to _____.

Commission file number: 001-37923

CRISPR THERAPEUTICS AG

(Exact name of Registrant as specified in its charter)

Switzerland	**Not Applicable**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
Baarerstrasse 14 6300 Zug, Switzerland	**Not Applicable**
(Address of principal executive offices)	**(zip code)**

+41 (0)41 561 32 77
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Shares, nominal value CHF 0.03	**CRSP**	**The Nasdaq Global Market**

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). YES ☒ NO ☐

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

Large Accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

As of May 5, 2022, there were 77,457,081 shares of registrant's common shares outstanding.

Throughout this Quarterly Report on Form 10-Q, the "Company," "CRISPR," "CRISPR Therapeutics," "we," "us," and "our," except where the context requires otherwise, refer to CRISPR Therapeutics AG and its consolidated subsidiaries.

"CRISPR Therapeutics®" standard character mark and design logo, "CTX001™," "CTX110™," "CTX120™," "CTX130™," and "CRISPR TX™" are trademarks and registered trademarks of CRISPR Therapeutics AG. All other trademarks and registered trademarks contained in this Quarterly Report on Form 10-Q are the property of their respective owners. Solely for convenience, trademarks, service marks and trade names referred to in this Quarterly Report on Form 10-Q may appear without the ® or ™ symbols and any such omission is not intended to indicate waiver of any such rights.

FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains "forward-looking statements" that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Quarterly Report on Form 10-Q are forward-looking statements. These statements are often identified by the use of words such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "predict," "project," "potential," "will," "would" or the negative or plural of these words or similar expressions or variations, although not all forward-looking statements contain these identifying words. Forward-looking statements in this Quarterly Report on Form 10-Q include, but are not limited to, statements about:

- *the safety, efficacy and clinical progress of our various clinical programs including those for CTX001™, CTX110™, CTX120™, CTX130™ and VCTX210;*
- *the status of clinical trials, development timelines and discussions with regulatory authorities related to product candidates under development by us and our collaborators;*
- *the initiation, timing, progress and results of our preclinical studies and clinical trials, including our ongoing clinical trials and any planned clinical trials for CTX001, CTX110, CTX120, CTX130 and VCTX210, and our research and development programs, including delays or disruptions in clinical trials, non-clinical experiments and investigational new drug application-enabling studies;*
- *the actual or potential benefits of U.S. Food and Drug Administration, or FDA, designations, such as orphan drug, fast track and regenerative medicine advanced therapy, or RMAT, or such European equivalents, including PRIority MEdicines, or PRIME, designation;*
- *our ability to advance product candidates into, and successfully complete, clinical trials;*
- *our plan to consolidate our various office and laboratory locations in the greater Boston area into a single location and to validate our cell therapy manufacturing facility to enable us to produce clinical cell therapy product supply in the future;*
- *our intellectual property coverage and positions, including those of our licensors and third parties as well as the status and potential outcome of proceedings involving any such intellectual property;*
- *our anticipated expenses, ability to obtain funding for our operations and the sufficiency of our cash resources;*
- *the therapeutic value, development, and commercial potential of CRISPR/Cas9 gene-editing technologies and therapies; and*
- *potential impacts due to the ongoing coronavirus pandemic such as delays, interruptions or other adverse effects to clinical trials, delays in regulatory review, manufacturing and supply chain interruptions, adverse effects on healthcare systems and disruption of the global economy, and the overall impact of the coronavirus pandemic on our business, financial condition and results of operations.*

Any forward-looking statements in this Quarterly Report on Form 10-Q reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and assumptions that could cause our actual results and the timing of certain events to differ materially from future results expressed or implied by the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those identified herein, and those discussed in the section titled "Risk Factors," set forth in Part II, Item 1A of this Quarterly Report on Form 10-Q, if any, our Annual Report on Form 10-K filed with the Securities and Exchange Commission, or SEC, on February 15, 2022, and in other SEC filings. You should not rely upon forward-looking statements as predictions of future events. Such forward-looking statements speak only as of the date of this report. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make or enter into.

You should read this Quarterly Report on Form 10-Q and the documents that we have filed as exhibits to this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results, performance or achievements may be materially different from what we expect. Except as required by law, we undertake no obligation to update any forward-looking statements to reflect events or circumstances after the date of such statements.

Investors and others should note that we announce material information to our investors using our investor relations website (https://crisprtx.gcs-web.com/), SEC filings, press releases, public conference calls and webcasts. We use these channels as well as social media to communicate with the public about our company, our business, our product candidates and other matters. It is possible that the information we post on social media could be deemed to be material information. Therefore, we encourage investors, the media, and others interested in our company to review the information we post on the social media channels listed on our investor relations website.

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PART I—FINANCIAL INFORMATION

Item 1. Financial Statements

CRISPR Therapeutics AG
Condensed Consolidated Balance Sheets
(unaudited, in thousands, except share and per share data)

	As of	
	March 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 683,906	$ 923,031
Marketable securities	1,537,355	1,456,098
Accounts receivable	143	305
Prepaid expenses and other current assets	39,212	38,079
Total current assets	2,260,616	2,417,513
Property and equipment, net	157,453	137,575
Intangible assets, net	112	125
Restricted cash	12,123	16,913
Operating lease assets	171,541	174,460
Other non-current assets	4,330	5,291
Total assets	$ 2,606,175	$ 2,751,877
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	$ 27,111	$ 14,816
Accrued expenses	72,632	91,003
Deferred revenue, current	—	1,011
Accrued tax liabilities	2,608	724
Operating lease liabilities	11,076	12,158
Other current liabilities	270	171
Total current liabilities	113,697	119,883
Deferred revenue, non-current	12,323	12,323
Operating lease liabilities, net of current portion	227,904	212,872
Other non-current liabilities	7,335	7,339
Total liabilities	361,259	352,417
Commitments and contingencies, see Note 6		
Shareholders' equity:		
Common shares, CHF 0.03 par value, 145,364,335 shares authorized at March 31, 2022 and December 31, 2021, 77,566,721 and 77,170,382 shares issued at March 31, 2022 and December 31, 2021, respectively, 77,386,405 and 76,990,066 shares outstanding at March 31, 2022 and December 31, 2021, respectively	2,407	2,391
Treasury shares, at cost, 180,316 shares at March 31, 2022 and at December 31, 2021	(63)	(63)
Additional paid-in capital	2,634,597	2,598,114
Accumulated deficit	(375,132)	(195,915)
Accumulated other comprehensive loss	(16,893)	(5,067)
Total shareholders' equity	2,244,916	2,399,460
Total liabilities and shareholders' equity	$ 2,606,175	$ 2,751,877

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

CRISPR Therapeutics AG
Condensed Consolidated Statements of Operations and Comprehensive Loss
(unaudited, in thousands, except share and per share data)

	Three Months Ended March 31,	
	2022	**2021**
Revenue:		
Collaboration revenue	$ 178	$ 202
Grant revenue	762	337
Total revenue	940	539
Operating expenses:		
Research and development	118,245	70,620
General and administrative	28,021	24,517
Collaboration expense, net	30,646	19,945
Total operating expenses	176,912	115,082
Loss from operations	(175,972)	(114,543)
Other income:		
Other income, net	363	1,955
Total other income, net	363	1,955
Net loss before income taxes	(175,609)	(112,588)
Provision for income taxes	(3,608)	(575)
Net loss	(179,217)	(113,163)
Foreign currency translation adjustment	(27)	5
Unrealized loss on marketable securities	(11,799)	(383)
Comprehensive loss	$ (191,043)	$ (113,541)
Net loss per common share — basic	$ (2.32)	$ (1.51)
Basic weighted-average common shares outstanding	77,098,319	75,005,187
Net loss per common share — diluted	$ (2.32)	$ (1.51)
Diluted weighted-average common shares outstanding	77,098,319	75,005,187

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

CRISPR Therapeutics AG
Condensed Consolidated Statements of Shareholders' Equity
(unaudited, in thousands, except share and per share data)

	Common Shares		Treasury Shares					
	Shares	CHF 0.03 Par Value	Shares	Amount, at cost	Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Shareholders' Equity
Balance at December 31, 2020	73,914,844	$ 2,277	195,316	$ (63)	$ 2,235,679	$ (573,576)	$ (83)	$ 1,664,234
Issuance of common shares, net of issuance costs of $5.4 million	1,353,121	45	—	—	222,130	—	—	222,175
Vesting of restricted shares	109,355	3	—	—	—	—	—	3
Exercise of vested options, net of issuance costs of $1.5 million	342,051	15	—	—	9,769	—	—	9,784
Purchase of common stock under ESPP	11,257	—	—	—	751	—	—	751
Stock-based compensation expense	—	—	—	—	22,092	—	—	22,092
Other comprehensive loss	—	—	—	—	—	—	(378)	(378)
Net loss	—	—	—	—	—	(113,163)	—	(113,163)
Balance at March 31, 2021	75,730,628	$ 2,340	195,316	$ (63)	$ 2,490,421	$ (686,739)	$ (461)	$ 1,805,498
Balance at December 31, 2021	76,990,066	$ 2,391	180,316	$ (63)	$ 2,598,114	$ (195,915)	$ (5,067)	$ 2,399,460
Vesting of restricted shares	123,564	4	—	—	—	—	—	4
Exercise of vested options, net of issuance costs of $0.2 million	261,280	12	—	—	9,998	—	—	10,010
Purchase of common stock under ESPP	11,495	—	—	—	740	—	—	740
Stock-based compensation expense	—	—	—	—	25,745	—	—	25,745
Other comprehensive loss	—	—	—	—	—	—	(11,826)	(11,826)
Net loss	—	—	—	—	—	(179,217)	—	(179,217)
Balance at March 31, 2022	77,386,405	$ 2,407	180,316	$ (63)	$ 2,634,597	$ (375,132)	$ (16,893)	$ 2,244,916

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

CRISPR Therapeutics AG
Condensed Consolidated Statements of Cash Flows
(unaudited, in thousands)

	Three Months Ended March 31,	
	2022	**2021**
Operating activities:		
Net loss	$ (179,217)	$ (113,163)
Reconciliation of net loss to net cash used in operating activities:		
Depreciation and amortization	6,039	2,715
Equity-based compensation	25,745	22,092
Other non-cash items, net	6,099	2,064
Changes in:		
Accounts receivable	162	(6)
Prepaid expenses and other assets	4,611	(5,068)
Accounts payable and accrued expenses	(1,616)	(5,770)
Deferred revenue	(762)	(539)
Operating lease assets and liabilities	3,854	778
Other liabilities, net	(154)	(3,766)
Net cash used in operating activities	(135,239)	(100,663)
Investing activities:		
Purchase of property, plant and equipment	(15,350)	(7,024)
Purchases of marketable securities	(323,140)	(323,975)
Maturities of marketable securities	223,975	163,101
Net cash used in investing activities	(114,515)	(167,898)
Financing activities:		
Proceeds from issuance of common shares, net of issuance costs	—	214,592
Proceeds from exercise of options and ESPP contributions, net of issuance costs	10,649	11,399
Net cash provided by financing activities	10,649	225,991
Effect of exchange rate changes on cash	(27)	5
Decrease in cash	(239,132)	(42,565)
Cash, cash equivalents and restricted cash, beginning of period	939,944	1,185,468
Cash, cash equivalents and restricted cash, end of period	$ 700,812	$ 1,142,903
Supplemental disclosure of non-cash investing and financing activities		
Property and equipment purchases in accounts payable and accrued expenses	$ 5,888	$ 8,847
Equity issuance costs in accounts payable and accrued expenses	$ 217	$ 2,868
Leasehold improvements paid directly by landlord	$ 13,015	$ —

	As of March 31,	
Reconciliation to amounts within the condensed consolidated balance sheets	**2022**	**2021**
Cash and cash equivalents	683,906	1,126,059
Prepaid expenses and other current assets	4,783	—
Restricted cash	12,123	16,844
Cash, cash equivalents and restricted cash at end of period	$ 700,812	$ 1,142,903

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

1. Basis of Presentation and Significant Accounting Policies

Basis of Presentation

The accompanying condensed consolidated financial statements are unaudited and have been prepared by the Company in accordance with accounting principles generally accepted in the United States of America, or U.S. GAAP.

The accompanying condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. The Company views its operations and manages its business in one operating segment, which is the business of discovering, developing and commercializing therapies derived from or incorporating genome-editing technology. Certain information and footnote disclosures normally included in the Company's annual financial statements have been condensed or omitted. These interim financial statements, in the opinion of management, reflect all normal recurring adjustments necessary for a fair presentation of the financial position and results of operations for the three-month interim periods ended March 31, 2022 and 2021.

The results of operations for the interim periods are not necessarily indicative of the results of operations to be expected for the full year. These interim financial statements should be read in conjunction with the audited financial statements for the year ended December 31, 2021, which are contained in the 2021 Annual Report on Form 10-K filed with the Securities and Exchange Commission, or the SEC, on February 15, 2022.

Beginning in the first quarter of 2022, collaboration costs under the Vertex Agreements accounted for under ASC 808, *Collaborative Agreements*, or ASC 808, are presented within "collaboration expense, net" in the condensed consolidated statements of operations and comprehensive loss. As a result, collaboration costs under the Vertex Agreements accounted for under ASC 808 for the period ending Mach 31, 2021 have been reclassified to conform to the current presentation. No subtotals in the prior interim period's consolidated condensed financial statements were impacted. Refer to Note 7 to these condensed consolidated financial statements for further discussion on the Vertex Agreements.

Use of Estimates

The preparation of financial statements in conformity with U.S. 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, revenue recognition, equity-based compensation expense and reported amounts of expenses during the period. Significant estimates in these consolidated financial statements have been made in connection with revenue recognition and equity-based compensation expense. 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. Changes in estimates are reflected in reported results in the period in which they become known.

Significant Accounting Policies

The significant accounting policies used in preparation of these condensed consolidated financial statements for the three months ended March 31, 2022 are consistent with those discussed in Note 2 to the consolidated financial statements in the Company's 2021 Annual Report on Form 10-K filed with the SEC on February 15, 2022.

New Accounting Pronouncements – Recently Adopted

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board, or FASB, or other standard setting bodies that the Company adopts as of the specified effective date. The Company does not believe that the adoption of recently issued standards have or may have a material impact on its consolidated financial statements and disclosures.

2. Marketable Securities

The following table summarizes cash equivalents and marketable securities held at March 31, 2022 and December 31, 2021 (in thousands), which are recorded at fair value. The table below excludes $138.8 million and $405.6 million of cash at March 31, 2022 and December 31, 2021, respectively.

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
March 31, 2022				
Cash equivalents:				
Money market funds	$ 416,688	$ —	$ —	$ 416,688
Corporate debt securities	11,827	—	(3)	11,824
Certificates of deposit	—	—	—	—
Commercial paper	116,606	1	(4)	116,603
Total cash equivalents	545,121	1	(7)	545,115
Marketable securities:				
U.S. Treasury securities	12,126	—	(269)	11,857
Corporate debt securities	1,166,163	3	(15,982)	1,150,184
Certificates of deposit	57,631	—	—	57,631
Government-sponsored enterprise securities	13,299	—	(236)	13,063
Commercial paper	305,033	5	(418)	304,620
Total marketable securities	1,554,252	8	(16,905)	1,537,355
Total cash equivalents and marketable securities	$ 2,099,373	$ 9	$ (16,912)	$ 2,082,470
December 31, 2021				
Cash equivalents:				
Money market funds	$ 507,386	$ —	$ —	$ 507,386
Corporate debt securities	—	—	—	—
Certificates of deposit	—	—	—	—
Commercial paper	9,997	—	(1)	9,996
Total cash equivalents	517,383	—	(1)	517,382
Marketable securities:				
U.S. Treasury securities	16,238	6	(52)	16,192
Corporate debt securities	1,173,659	10	(4,903)	1,168,766
Certificates of deposit	45,164	—	—	45,164
Government-sponsored enterprise securities	13,334	—	(77)	13,257
Commercial paper	212,805	—	(86)	212,719
Total marketable securities	1,461,200	16	(5,118)	1,456,098
Total cash equivalents and marketable securities	$ 1,978,583	$ 16	$ (5,119)	$ 1,973,480

As of March 31, 2022 and December 31, 2021, the aggregate fair value of marketable securities that were in an unrealized loss position for less than twelve months was $534.9 million and $1,311.6 million, respectively. As of March 31, 2022 and December 31, 2021, the aggregate fair value of marketable securities that were in an unrealized loss position for more than twelve months was $9.5 million and $4.6 million, respectively. The Company has recorded a net unrealized loss of $11.8 million and $0.4 million during the three months ended March 31, 2022 and 2021 respectively, related to its debt securities, which is included in comprehensive loss on the condensed consolidated statements of operations and comprehensive loss.

The Company determined that there is no material credit risk associated with the above investments as of March 31, 2022. The Company has the intent and ability to hold such securities until recovery. As a result, the Company did not record any charges for credit-related impairments for its marketable securities for the three months ended March 31, 2022 and 2021. No available-for-sale debt securities held as of March 31, 2022 had remaining maturities greater than thirty months.

3. Fair Value Measurements

The following tables present information about the Company's financial assets measured at fair value on a recurring basis and indicate the fair value hierarchy classification of such fair values as of March 31, 2022 and December 31, 2021 (in thousands):

	Fair Value Measurements at March 31, 2022			
	Total	Level 1	Level 2	Level 3
Cash and cash equivalents:				
Cash	$ 138,791	$ 138,791	$ —	$ —
Money market funds	416,688	416,688	—	—
Corporate debt securities	11,824	—	11,824	—
Certificates of deposit	116,603	—	116,603	—
Commercial paper	—	—	—	—
Marketable securities:				
U.S. Treasury securities	11,857	—	11,857	—
Corporate debt securities	1,150,184	—	1,150,184	—
Certificates of deposit	57,631	—	57,631	—
Government-sponsored enterprise securities	13,063	—	13,063	—
Commercial paper	304,620	—	304,620	—
Other non-current assets	2,212	—	—	2,212
Total	$ 2,223,473	$ 555,479	$ 1,665,782	$ 2,212

	Fair Value Measurements at December 31, 2021			
	Total	Level 1	Level 2	Level 3
Cash and cash equivalents:				
Cash	$ 405,648	$ 405,648	$ —	$ —
Money market funds	507,386	507,386	—	—
Corporate debt securities	—	—	—	—
Certificates of deposit	—	—	—	—
Commercial paper	9,997	—	9,997	—
Marketable securities:				
U.S. Treasury securities	16,192	—	16,192	—
Corporate debt securities	1,168,766	—	1,168,766	—
Certificates of deposit	45,164	—	45,164	—
Government-sponsored enterprise securities	13,257	—	13,257	—
Commercial paper	212,719	—	212,719	—
Other non-current assets	2,212	—	—	2,212
Total	$ 2,381,341	$ 913,034	$ 1,466,095	$ 2,212

Marketable securities classified as Level 2 within the valuation hierarchy generally consist of U.S. treasury securities and government agency securities, corporate bonds, and commercial paper. The Company estimates the fair values of these marketable securities by taking into consideration valuations obtained from third-party pricing sources.

The Company holds equity securities classified as Level 3 which are not material to the Company's financial position.

4. Property and Equipment, net

Property and equipment, net, consists of the following (in thousands):

	As of	
	March 31, 2022	December 31, 2021
Computer equipment	$ 1,943	$ 1,757
Furniture, fixtures and other	4,371	4,371
Laboratory equipment	34,705	30,123
Leasehold improvements	86,401	86,735
Construction work in process	73,866	52,396
Total property and equipment, gross	201,286	175,382
Accumulated depreciation	(43,833)	(37,807)
Total property and equipment, net	$ 157,453	$ 137,575

Depreciation expense for the three months ended March 31, 2022 and 2021 was $6.0 million and $2.7 million, respectively.

5. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	As of	
	March 31, 2022	December 31, 2021
Payroll and employee-related costs	$ 8,780	$ 23,661
Research costs	49,925	47,986
Licensing fees	533	138
Professional fees	4,456	4,720
Intellectual property costs	4,345	6,120
Accrued property and equipment	2,321	7,113
Other	2,272	1,265
Total	$ 72,632	$ 91,003

6. Commitments and Contingencies

Leases

Refer to Note 7 to the consolidated financial statements in the Company's 2021 Annual Report on Form 10-K filed with the SEC on February 15, 2022 for discussion on the Company's lease arrangements.

Litigation

In the ordinary course of business, the Company is from time to time involved in lawsuits, investigations, proceedings and threats of litigation related to, among other things, the Company's intellectual property estate (including certain in-licensed intellectual property), commercial arrangements and other matters. Such proceedings may include quasi-litigation, inter partes administrative proceedings in the U.S. Patent and Trademark Office and the European Patent Office involving the Company's intellectual property estate including certain in-licensed intellectual property. The outcome of any of the foregoing, regardless of the merits, is inherently uncertain. In addition, litigation and related matters are costly and may divert the attention of Company's management and other resources that would otherwise be engaged in other activities. If the Company is unable to prevail in any such proceedings, the Company's business, results of operations, liquidity and financial condition could be adversely affected.

Letters of Credit

As of March 31, 2022, the Company had restricted cash of $16.9 million, representing letters of credit securing the Company's obligations under certain leased facilities. The letters of credit are secured by cash held in a restricted depository account, with $4.8 million included in "Prepaid expenses and other current assets" and $12.1 million included in "Restricted cash" on the Company's condensed consolidated balance sheets as of March 31, 2022.

Research, Manufacturing, License and Intellectual Property Agreements

The Company has engaged several research institutions and companies to identify new delivery strategies and applications of the Company's gene-editing technology. The Company is also a party to a number of license agreements which require significant upfront payments and may be required to make future royalty payments and potential milestone payments from time to time. In addition, the Company is also a party to intellectual property agreements, which require maintenance and milestone payments from time to time. Further, the Company is a party to a number of manufacturing agreements that require upfront payments for the future performance of services.

In association with these agreements, on a product-by-product basis, the counterparties are eligible to receive up to low eight-digit potential payments upon specified research, development and regulatory milestones. In addition, on a product-by-product basis, the counterparties are eligible to receive potential commercial milestone payments based on specified annual sales thresholds. The potential payments are low-single digit percentages of the specified annual sales thresholds. The counterparties are also eligible to receive low single-digit royalties on future net sales.

Under certain circumstances and if certain contingent future events occur, Vertex Pharmaceuticals Incorporated and certain of its subsidiaries, or Vertex, is eligible to receive up to $395.0 million in potential specified research, development, regulatory and commercial milestones and tiered single-digit percentage royalties on future net sales related to a specified target under an amendment to the 2015 Collaboration Agreement defined in Note 7 below. In addition, Vertex has the option to conduct research at their own cost in certain defined areas that, if beneficial to the CTX001 program and ultimately achieves regulatory approval, then the Company could owe Vertex certain milestone payments aggregating to high eight digits, subject to certain limitations on the profitability of the CTX001 program. Refer to Note 7 for further discussion on the Company's arrangements with Vertex.

7. Significant Contracts

Agreements with Vertex Pharmaceuticals Incorporated and certain of its subsidiaries

Summary

On October 26, 2015, the Company entered into a strategic collaboration, option and license agreement, or the 2015 Collaboration Agreement, with Vertex. The 2015 Collaboration Agreement is focused on the use of the Company's CRISPR/Cas9 gene-editing technology to discover and develop potential new treatments aimed at the underlying genetic causes of human disease.

On December 12, 2017, the Company and Vertex entered into Amendment No. 1 to the 2015 Collaboration Agreement, or Amendment No. 1, and the Joint Development Agreement, or the JDA. Amendment No. 1, among other things, modified certain definitions and provisions of the 2015 Collaboration Agreement to make them consistent with the JDA and clarified how many options are exercised (or deemed exercised) in connection with certain targets specified under the 2015 Collaboration Agreement. Amendment No. 1 also amended other provisions of the 2015 Collaboration Agreement, including the expiration terms.

In connection with the 2015 Collaboration Agreement, Vertex made a nonrefundable upfront payment of $75.0 million. Under the 2015 Collaboration Agreement, Vertex agreed to fund the discovery activities conducted pursuant to the agreement while retaining options to co-exclusive and exclusive licenses. In December 2017, upon execution of the JDA and Amendment No. 1, Vertex exercised its option to obtain a co-exclusive license to develop and commercialize hemoglobinopathy and beta-globin targets. As such, for potential hemoglobinopathy treatments, including treatments for sickle cell disease, the Company and Vertex agreed to share equally all research and development costs and worldwide revenues. In connection with the JDA, the Company received a $7.0 million up-front payment from Vertex and subsequently received a one-time low seven-digit milestone payment upon the dosing of the second patient in a clinical trial with the initial product candidate. In addition, upon execution of the JDA and Amendment No. 1, it was clarified that Vertex may elect to license up to four remaining targets, for which it will lead global development and commercialization activities, and the Company received the right to receive up to $420.0 million in development, regulatory and commercial milestones and royalties on net product sales for each of the targets (inclusive of $10 million due upon exercise of each exclusive option).

In June 2019, the Company and Vertex entered into a series of agreements, which closed in the second quarter of 2019, including a strategic collaboration and license agreement, or the 2019 Collaboration Agreement, for the development and commercialization of products for the treatment of Duchenne muscular dystrophy, or DMD, and Myotonic Dystrophy Type 1, or DM1. Under the terms of the 2019 Collaboration Agreement, the Company received an upfront, nonrefundable payment of $175.0 million. In addition, the Company was initially eligible to receive potential aggregate payments of up to $825.0 million based upon the successful achievement of specified research, development, regulatory and commercial milestones for the DMD and DM1 programs.

The Company is also eligible to receive tiered royalties on future net sales on any products that may result from the 2019 Collaboration Agreement. For the DMD program, Vertex is responsible for all research, development, manufacturing and commercialization activities and all related costs. For the DM1 program, the Company performed specified guide RNA research and Vertex is responsible for all other research, development, manufacturing and commercialization costs. Upon Investigational New Drug, or IND, application filing, the Company has the option to forego the DM1 milestones and royalties, and instead, co-develop and co-commercialize all DM1 products globally in exchange for payment of 50% of research and development costs incurred by Vertex from the effective date of the agreement through IND filing.

In connection with the execution of the 2019 Collaboration Agreement, the Company and Vertex entered into a second amendment to the 2015 Collaboration Agreement, or Amendment No. 2. Among other things, Amendment No. 2 modified certain definitions and provisions of the 2015 Collaboration Agreement to make them consistent with the 2019 Collaboration Agreement and set forth the number and identity of the collaboration targets under the 2015 Collaboration Agreement. The Company and Vertex agreed that one of the four remaining options under the 2015 Collaboration Agreement, as amended, would not be exercised; instead, the Company reacquired the exclusive rights and agreed to conduct research and development activities for the specified target. Vertex will have the option to co-develop and co-commercialize the specified target upon IND filing in exchange for payment of 50% of research and development costs incurred by the Company from the effective date of the agreement through IND filing. If Vertex does not exercise its option to co-develop and co-commercialize the specified target, Vertex is eligible to receive up to $395.0 million in potential specified research, development, regulatory and commercial milestones and tiered single-digit royalties on future net sales.

In October 2019, Vertex exercised the remaining three options granted to it under the 2015 Collaboration Agreement to exclusively license the collaboration targets developed under the 2015 Collaboration Agreement, resulting in a payment of $30.0 million to the Company in the fourth quarter of 2019. In addition, the Company achieved the first milestone under the 2019 Collaboration Agreement in the first quarter of 2020 and, in connection therewith, received a payment of $25.0 million in April 2020. The Company achieved the second milestone under the 2019 Collaboration Agreement in the fourth quarter of 2021 and, in connection therewith, received a payment of $12.5 million in December 2021. As of March 31, 2022, the Company is eligible to receive remaining potential future milestones of $775.0 million under the 2019 Collaboration Agreement.

In April 2021, the Company and Vertex agreed to amend and restate the JDA and entered into an Amended and Restated Joint Development and Commercialization Agreement, or the "A&R Vertex JDCA," pursuant to which the parties agreed to, among other things, (a) adjust the governance structure for the collaboration and adjust the responsibilities of each party thereunder, whereby Vertex shall lead and have all decision making (i.e., control) in relation to the CTX001 program prospectively; (b) adjust the allocation of net profits and net losses between the parties with respect to CTX001 only, which will be allocated 40% to the Company and 60% to Vertex, prospectively; and (c) exclusively license (subject to the Company's reserved rights to conduct certain activities) certain intellectual property rights to Vertex relating to the specified product candidates and products (including CTX001) that may be researched, developed, manufactured and commercialized on a worldwide basis under such agreement. The transaction contemplated by the A&R Vertex JDCA closed in the second quarter of 2021. The Company is providing certain specified transition services to Vertex in connection with the agreement.

In connection with the closing of the transaction contemplated by the A&R Vertex JDCA, the Company received a $900.0 million up-front payment from Vertex. Additionally, the Company is eligible to receive a one-time $200.0 million milestone payment upon receipt by Vertex of the first marketing approval of the initial product candidate from the U.S. Food and Drug Administration or the European Commission. With respect to CTX001 only, the net profits and net losses, as applicable, incurred under the A&R Vertex JDCA through July 1, 2021 in connection with the initial shared product (i.e., CTX001) were shared equally between the Company and Vertex, and beginning July 1, 2021, the net profits and net losses, as applicable, incurred under the A&R Vertex JDCA are allocated 40% to the Company and 60% to Vertex. Additionally, the A&R Vertex JDCA allows the Company to defer a portion of its share of costs under the arrangement if spending on the CTX001 program exceeds specified amounts. Any deferred amounts are only payable to Vertex as an offset against future profitability of the CTX001 program and the amounts payable are capped at a specified maximum amount per year.

Accounting for the Vertex Agreements

The 2015 Collaboration Agreement, Amendment No. 1, and JDA are collectively the "2015 Agreements" and the 2019 Collaboration Agreement and Amendment No. 2. are collectively the "2019 Agreements." The 2015 Collaboration Agreement, Amendment No. 1, Amendment No. 2, JDA, A&R Vertex JDCA and 2019 Collaboration Agreement are collectively the "Vertex Agreements."

The Vertex Agreements include components of a customer-vendor relationship as defined under ASC 606, *Revenue from Contracts with Customers*, or ASC 606, collaborative arrangements as defined under ASC 808, *Collaborative Agreements*, or ASC 808, and research and development costs as defined under ASC 730, *Research and Development*, or ASC 730. Additionally, the A&R Vertex JDCA allows the Company to defer a portion of its share of costs under the arrangement if spending on the CTX001 program exceeds specified amounts, which are only payable to Vertex as an offset against future profitability of the CTX001 program up to a maximum amount per year.

Accounting Analysis Under ASC 606

Accounting for the A&R Vertex JDCA

Identification of the Contract

The A&R Vertex JDCA represented a contractual modification to the JDA. For accounting purposes, the A&R Vertex JDCA was treated as a separate contract.

Identification of Performance Obligations

The Company concluded the A&R Vertex JDCA contained a single material promise, an exclusive worldwide license granting Vertex an additional 10% economic interest in the CTX001 program and the right to control development and commercialization of CTX001, or the "CTX001 Exclusive License." The Company concluded the CTX001 Exclusive License was both capable of being distinct and distinct within the context of the A&R Vertex JDCA, and the CTX001 Exclusive License was sold at its estimated standalone selling price, or "ESSP." As such, the CTX001 Exclusive License represented a separate performance obligation.

Determination of Transaction Price

The transaction price was comprised of the upfront payment of $900.0 million. The Company determined that all other possible variable consideration resulting from milestones and royalties discussed above was fully constrained at the time of the transaction. The Company will reevaluate the transaction price in each reporting period.

Allocation of Transaction Price to Performance Obligations

The selling price of the performance obligation was determined based on the Company's ESSP. The Company developed the ESSP for the CTX001 Exclusive License 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 ESSP for the CTX001 Exclusive License was determined to be approximately $900.0 million. The ESSP was determined based on 10% of the probability and present value adjusted cash flows from projected worldwide net profit for CTX001 based on probability assessments, projections based on internal forecasts, industry data, and information from other guideline companies within the same industry and other relevant factors. As the Company determined the CTX001 Exclusive License was the only performance obligation, the entire transaction price was allocated to the CTX001 Exclusive License. The aforementioned ESSP reflects the level of risk and expected probability of success inherent in the nature of the associated research area.

Recognition of Revenue

The Company determined that the CTX001 Exclusive License represented functional intellectual property, as the intellectual property provides Vertex with the ability to perform a function or task in the form of research and development, manufacturing and commercialization. As such, the revenue related to the CTX001 Exclusive License was recognized at the point in time, which was upon transfer in the second quarter of 2021.

Accounting for the 2019 Agreements

The 2019 Agreements represented a contract modification to the 2015 Agreements. As a result, the 2019 Agreements and the 2015 Agreements are combined for accounting purposes and treated as a single arrangement. Transactions under the 2019 Agreements were not material for the three months ended March 31, 2022 and 2021.

The Company determined that all possible variable consideration remaining under the 2019 Agreements resulting from milestones and royalties discussed above was fully constrained as of March 31, 2022. The Company will re-evaluate the transaction price in each reporting period.

Revenue recognized in connection with the Vertex Agreements

Revenue recognized under the Vertex Agreements for the three months ended March 31, 2022 and 2021, respectively, was not material.

As of March 31, 2022 and December 31, 2021, there was no current deferred revenue related to the collaboration with Vertex. As of March 31, 2022, there was $12.3 million of non-current deferred revenue related to the collaboration with Vertex, which is unchanged from December 31, 2021. The transaction price allocated to the remaining performance obligations was $12.3 million.

Future Milestones under the Vertex Agreements

The Company has evaluated the milestones that may be received in connection with the Vertex Agreements. As discussed above, the Company is eligible to receive up to $410.0 million in additional development, regulatory and commercial milestones and royalties on net product sales for each of the three collaboration targets that Vertex licensed in the fourth quarter of 2019. Each milestone is payable only once per collaboration target, regardless of the number of products directed to such collaboration target that achieve the relevant milestone event.

The Company is eligible to receive additional potential future payments of up to $775.0 million based upon the successful achievement of specified development, regulatory and commercial milestones for the DMD and DM1 programs. The Company is also eligible to receive tiered royalties on future net sales on any products that may result from this collaboration; however, the Company has the option to forego the DM1 milestones and royalties to co-develop and co-commercialize all DM1 products globally.

The Company is eligible to receive additional potential future payments of up to $200.0 million upon receipt by Vertex of the first marketing approval of the initial product candidate from the U.S. Food and Drug Administration or the European Commission. In addition, the Company has the option to conduct research at their own cost in certain defined areas that, if beneficial to the CTX001 program and CTX001 ultimately achieves regulatory approval in such areas, then the Company could be entitled to certain milestone payments aggregating to high eight digits from Vertex.

Each of the remaining milestones are fully constrained as of March 31, 2022. There is uncertainty that the events to obtain the research and developmental milestones will be achieved given the nature of clinical development and the stage of the CRISPR/Cas9 technology. The remaining research, development and regulatory milestones will be constrained until it is probable that a significant revenue reversal will not occur. Commercial milestones and royalties relate predominantly to a license of intellectual property and are determined by sales or usage-based thresholds. The commercial milestones and royalties are accounted for under the royalty recognition constraint and will be accounted for as constrained variable consideration. The Company applies the royalty recognition constraint for each commercial milestone and will not recognize revenue for each until the subsequent sale of a licensed product (achievement of each) occurs.

Accounting Analysis under ASC 808

In connection with the Vertex Agreements, the Company identified the following collaborative elements, which are accounted for under ASC 808: (i) development and commercialization services for shared products, including any transition services related to CTX001 under the A&R Vertex JDCA; (ii) R&D Services for follow-on products; and (iii) committee participation. The related impact of the cost sharing is included within collaboration expense, net, in the condensed consolidated statements of operations and comprehensive loss.

During the three months ended March 31, 2022 and 2021, the Company recognized $30.6 million and $19.9 million of collaboration expense, net, related to the Vertex Agreements, respectively. Collaboration expense, net, was net of $7.4 million and $10.6 million of reimbursements from Vertex, respectively.

8. Share Capital

The Company had 145,364,335 authorized common shares as of March 31, 2022, with a par value of CHF 0.03 per share. Share Capital consisted of the following:

		As of	
Type of Share Capital	**Conditional Capital**	**March 31, 2022**	**December 31, 2021**
Common shares	Registered share capital	82,028,328	80,321,227
Common shares	Authorized share capital	39,316,975	39,316,975
Common shares	Conditional share capital - Bonds or similar debt instruments	4,919,700	4,919,700
Common shares	Conditional share capital - Employee benefit plans	19,099,332	20,806,433
	Total	145,364,335	145,364,335

Common Share Issuances

At-the-Market Offering

In August 2019, the Company entered into an Open Market Sale Agreement[SM] with Jefferies LLC, or Jefferies, under which the Company was able to offer and sell, from time to time at its sole discretion through Jefferies, as its sales agent, its common shares, or the August 2019 Sales Agreement.

In January 2021, in connection with the August 2019 Sales Agreement, the Company filed a prospectus supplement with the SEC to offer and sell, from time to time, common shares having aggregate gross proceeds of up to $600.0 million. In July 2021, the Company filed a new prospectus supplement with the SEC, which replaced the previous prospectus supplement filed in January 2021, to offer and sell, from time to time, common shares having aggregate gross proceeds of up to $419.8 million, or the 2021 ATM. As of March 31, 2022, the Company has issued and sold an aggregate of 1.1 million common shares under the 2021 ATM at an average price of $169.82 per share for aggregate proceeds of $177.8 million, which were net of equity issuance costs of $2.4 million. No shares were issued and sold under the 2021 ATM for the three months ended March 31, 2022.

9. Stock-based Compensation

During the three months ended March 31, 2022 and 2021, the Company recognized the following stock-based compensation expense (in thousands):

	Three Months Ended March 31,	
	2022	2021
Research and development	$ 14,589	$ 12,845
General and administrative	11,156	9,247
Total	$ 25,745	$ 22,092

Stock option activity

The following table summarizes stock option activity for the three months ended March 31, 2022:

	Shares	Weighted-average exercise price per share
Outstanding at December 31, 2021	7,812,982	$ 58.07
Granted	820,189	58.62
Exercised	(261,280)	39.17
Cancelled or forfeited	(151,433)	78.48
Outstanding at March 31, 2022	8,220,458	$ 58.35
Exercisable at March 31, 2022	4,757,990	$ 43.59
Vested and expected to vest at March 31, 2022	8,220,458	$ 58.35

As of March 31, 2022, total unrecognized compensation expense related to stock options was $157.6 million, which the Company expects to recognize over a remaining weighted-average period of 2.8 years.

Restricted stock activity

The following table summarizes restricted stock activity for the three months ended March 31, 2022:

	Restricted Stock	Weighted-Average Grant Date Fair Value
Unvested balance as of December 31, 2021	934,175	$ 100.14
Granted	361,896	58.55
Vested	(123,564)	83.94
Cancelled or forfeited	(25,143)	109.89
Unvested balance as of March 31, 2022	1,147,364	$ 88.56

As of March 31, 2022, total unrecognized compensation expense related to unvested restricted common shares was $81.6 million, which the Company expects to recognize over a remaining weighted-average vesting period of 2.7 years.

10. Net Loss Per Share Attributable to Common Shareholders

Basic net loss per share is calculated by dividing net loss attributable to common shareholders by the weighted-average number of common shares outstanding during the period. Diluted net loss per share is calculated by dividing the net loss attributable to common shareholders by the weighted-average number of common share equivalents outstanding for the period, including any dilutive effect from outstanding stock options and warrants using the treasury stock method. The Company's net loss is net loss attributable to common shareholders for all periods presented.

The following common stock equivalents were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect (in thousands):

	Three Months Ended March 31,	
	2022	**2021**
Outstanding options	8,220,458	8,572,663
Unvested restricted common shares	1,147,364	1,052,379
ESPP	10,969	10,594
Total	9,378,791	9,635,636

11. Income Taxes

During the three months ended March 31, 2022 and 2021, the Company recorded an income tax provision of $3.6 million and a provision of $0.6 million, respectively, representing an effective tax rate of -2.1% and -0.5%, respectively. The income tax provision is primarily attributable to the year-to-date pre-tax income earned by the Company's U.S. subsidiary. The decrease in the rate for the three months ended March 31, 2022 is primarily attributable to the requirement to capitalize research and development costs for tax purposes under the 2017 "Tax Cuts and Jobs Act" (TCJA) which impacts the Company's permanent tax adjustments and the Company's valuation allowance assessment. The difference in the statutory tax rate and effective tax rate is primarily a result of the jurisdictional mix of earnings, research credits generated, and the valuation allowance recorded against certain deferred tax assets. The Company maintains a valuation allowance against certain deferred tax assets that are not more-likely-than-not realizable.

Item 2. 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 in conjunction with (i) our unaudited condensed consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and (ii) our audited consolidated financial statements and related notes and management's discussion and analysis of financial condition and results of operations included in our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the Securities and Exchange Commission, or the SEC, on February 15, 2022. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business and impact and potential impacts on our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including, without limitation, those factors set forth in the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2021 and the "Risk Factors" section of subsequent Quarterly Reports on Form 10-Q, our actual results or timing of certain events could differ materially from the results or timing described in, or implied by, these forward-looking statements.

Special Note About Coronavirus (COVID-19)

Since March 2020, we have been evaluating the actual and potential business impacts related to the outbreak of a novel strain of virus named SARS-CoV-2 (severe acute respiratory syndrome 2), or coronavirus, which causes coronavirus disease, or COVID-19. As a result of the ongoing coronavirus pandemic, we have experienced, and may further experience, disruptions, pauses and/or delays that have and could further adversely impact our business operations, and/or associated timelines. We maintain temporary work-from-home procedures for all employees other than for those personnel and contractors who perform essential activities that must be completed on-site. If negative developments relating to the coronavirus pandemic continue, including "periodic resurgence" and additional "waves", we may be required to restrict on-site staff at our offices and laboratories again and at times have limited access to our offices on a temporary and intermittent basis; with respect to our hemoglobinopathies clinical trials, we may elect to pause patient dosing in certain of our trials again if ICU beds and related healthcare resources become significantly constrained again or governmental authorities impose additional business or travel restrictions; with respect to our immuno-oncology clinical trials, investigators participating in our clinical trials may not want to take the risk of exposing cancer patients to the coronavirus since the dosing of patients is conducted within an in-patient setting; and certain aspects of our supply chain could be disrupted if our third party suppliers and manufacturers paused their operations again in response to such negative developments and/or as a result of national and local regulations. The ultimate impact of the coronavirus pandemic on our business operations remains uncertain and subject to change and will depend on future developments, which cannot be accurately predicted. We will continue to monitor the situation closely.

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 such diseases. We believe that our scientific expertise, together with our approach, may enable an entirely new class of highly active and potentially curative therapies for patients for whom current biopharmaceutical approaches have had limited success.

We have established a portfolio of therapeutic programs across a broad range of disease areas including hemoglobinopathies, oncology, regenerative medicine and rare diseases.

Hemoglobinopathies

Our lead product candidate, CTX001, is an investigational, autologous, gene-edited hematopoietic stem cell therapy that is being evaluated for the treatment of transfusion-dependent beta thalassemia, or TDT, and severe sickle cell disease, or SCD. CTX001 is being developed under a joint development and commercialization agreement between us and Vertex Pharmaceuticals Incorporated and certain of its subsidiaries, or Vertex.

We and Vertex are investigating CTX001 in two ongoing Phase 3 open-label clinical trials that are designed to assess the safety and efficacy of a single dose of CTX001 in patients ages 12 to 35 with TDT (CLIMB THAL-111) or SCD (CLIMB SCD-121), respectively. The first two patients in each trial were treated sequentially and, following data from the initial two patients indicating successful engraftment and an acceptable safety profile, the corresponding trial opened for concurrent dosing. CLIMB THAL-111 and CLIMB SCD-121 are designed to follow patients for approximately two years after infusion. Each patient will be asked to participate in a long-term, open-label follow-up trial, CLIMB-131, to evaluate the safety and efficacy of CTX001 in patients who received CTX001. CLIMB-131 is designed to follow participants for up to 15 years after CTX001 infusion. Enrollment is complete for both CLIMB THAL-111 and CLIMB SCD-121.

In the second quarter of 2021, at the European Hematology Association Congress, we presented updated clinical data from CLIMB THAL-111 and CLIMB SCD-121 for the first fifteen patients with TDT and first seven patients with SCD treated with CTX001 who had reached at least three months of follow-up after CTX001 dosing.

We and Vertex have also initiated two additional Phase 3 clinical trials of CTX001 in pediatric patients with TDT and SCD.

CTX001 has been granted a number of regulatory designations from the FDA, including RMAT, Fast Track, Orphan Drug, and Rare Pediatric Disease designations for the treatment of both TDT and SCD. CTX001 has also been granted Orphan Drug Designation from the European Commission, as well as PRIME designation from the European Medicines Agency, for the treatment of both TDT and SCD.

Immuno-Oncology

In addition, we are developing our own portfolio of CAR-T cell product candidates based on our gene-editing technology.

CTX110. Our lead immuno-oncology product candidate, CTX110, is a healthy donor-derived gene-edited allogeneic CAR-T investigational therapy targeting Cluster of Differentiation 19, or CD19. CTX110 is being investigated in an ongoing Phase 1 single-arm, multi-center, open-label clinical trial, CARBON, that is designed to assess the safety and efficacy of several dose levels of CTX110 in adult patients with relapsed or refractory B-cell malignancies who have received at least two prior lines of therapy. CTX110 has been granted RMAT designation by the FDA.

In the fourth quarter of 2021, we released updated clinical data from the ongoing CARBON trial for 26 patients treated with CTX110 who had reached at least 28 days of follow-up.

CTX120. CTX120 is a healthy donor-derived gene-edited allogeneic CAR-T investigational therapy targeting B-cell maturation antigen. CTX120 is being investigated in an ongoing Phase 1 single-arm, multi-center, open-label clinical trial that is designed to assess the safety and efficacy of several dose levels of CTX120 for the treatment of relapsed or refractory multiple myeloma. CTX120 has received Orphan Drug Designation from the FDA.

CTX130. CTX130 is a healthy donor-derived gene-edited allogeneic CAR-T investigational therapy targeting Cluster of Differentiation 70, or CD70, an antigen expressed on various solid tumors and hematologic malignancies. CTX130 is being developed for the treatment of both solid tumors, such as renal cell carcinoma, and T-cell and B-cell hematologic malignancies. CTX130 is being investigated in two ongoing independent Phase 1 single-arm, multi-center, open-label clinical trials that are designed to assess the safety and efficacy of several dose levels of CTX130 for the treatment of relapsed or refractory renal cell carcinoma and various types of lymphoma, respectively. CTX130 for the treatment of T-cell lymphoma has received Orphan Drug Designation from the FDA.

Regenerative Medicine

Regenerative medicine, or the use of stem cells to repair or replace tissue or organ function lost due to disease, damage or age, holds the potential to treat both rare and common diseases. We are pursuing gene-editing approaches to allow allogeneic use of stem cell-derived therapies by enabling immune evasion, improving existing cell function and directing cell fate using CRISPR/Cas9.

Our first major effort in this area is in diabetes, and we and ViaCyte, Inc., or ViaCyte, are advancing a program as part of a strategic collaboration for the discovery, development, and commercialization of gene-edited stem cell therapies for the treatment of diabetes.

VCTX210. VCTX210 is an investigational, allogeneic, gene-edited, immune-evasive, stem cell-derived product candidate for the treatment of type 1 diabetes, or T1D, developed by applying our gene-editing technology to ViaCyte's proprietary stem cell capabilities. We and ViaCyte are investigating VCTX210 in an ongoing Phase 1 clinical trial that is designed to assess VCTX210's safety, tolerability, and immune evasion in patients with T1D.

In Vivo

In addition to our *ex vivo* programs, we are pursuing a number of *in vivo* gene-editing programs. Our initial *in vivo* applications target diseases of the liver, lung, muscle and central nervous system and leverage well-established delivery technologies for gene-based therapeutics, such as lipid nanoparticle-based delivery vehicles, or LNPs, and adeno-associated viral vectors, or AAV vectors.

Partnerships

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 technologies and/or disease-area expertise. We maintain broad partnerships to develop gene editing-based therapeutics in specific disease areas.

Vertex. We established our initial collaboration agreement in 2015 with Vertex, which focused on TDT, SCD, cystic fibrosis and select additional indications. In December 2017, we entered into a joint development and commercialization agreement with Vertex pursuant to which, among other things, we are co-developing and preparing to co-commercialize CTX001 for TDT and SCD. In April 2021, we and Vertex agreed to amend and restate our existing joint development and commercialization agreement, pursuant to which, among other things, we will continue to develop and prepare to commercialize CTX001 for TDT and SCD in partnership with Vertex. We also entered into a strategic collaboration and license agreement with Vertex in June 2019 for the development and commercialization of products for the treatment of Duchenne muscular dystrophy and myotonic dystrophy type 1.

ViaCyte. We entered into a research and collaboration agreement in September 2018 with ViaCyte to pursue the discovery, development and commercialization of gene-edited allogeneic stem cell therapies for the treatment of diabetes and in July 2021, we entered into a joint development and commercialization agreement with ViaCyte. Under the joint development and commercialization agreement, we and ViaCyte will jointly develop and commercialize product candidates and shared products for use in the treatment of diabetes type 1, diabetes type 2 and insulin dependent/requiring diabetes throughout the world.

Bayer. In the fourth quarter of 2019, we entered into a series of transactions, or the Bayer Transaction, pursuant to which we and Bayer terminated our 2015 agreement, which created the joint venture, Casebia Therapeutics Limited Liability Partnership, or Casebia, to discover, develop and commercialize CRISPR/Cas9 gene-editing therapeutics to treat the genetic causes of bleeding disorders, autoimmune disease, blindness, hearing loss and heart disease. In connection thereto, Casebia became a wholly-owned subsidiary of ours. We and Bayer also entered into a new option agreement pursuant to which Bayer has an option to co-develop and co-commercialize two products for the diagnosis, treatment or prevention of certain autoimmune disorders, eye disorders, or hemophilia A disorders for a specified period of time, or, under certain circumstances, exclusively license such optioned products.

Nkarta. In the second quarter of 2021, we entered into a research and collaboration agreement with Nkarta, Inc., or Nkarta, to bring together our gene editing technology and T-cell expertise with Nkarta's leading natural killer, or NK, cell discovery, development and manufacturing capabilities. Under the collaboration, we and Nkarta are co-developing and co-commercializing two donor-derived, gene-edited CAR-NK cell product candidates, one of which targets CD70, and a product candidate combining NK and T cells.

Capsida. In the second quarter of 2021, we entered into a strategic collaboration agreement with Capsida Biotherapeutics, Inc., or Capsida, to develop in vivo gene editing therapies delivered with engineered AAV vectors for the treatment of amyotrophic lateral sclerosis, or ALS, and Friedreich's ataxia. Under the agreement, we lead research and development of the Friedreich's ataxia program and perform gene-editing activities for both programs, and Capsida leads research and development of the ALS program and conducts capsid engineering for both programs. Capsida's high-throughput AAV engineering platform aims to generate capsids optimized to target specific tissue types and limits transduction of tissues and cell types that are not relevant to the target disease, potentially improving the activity and tolerability of our gene editing investigational therapies. We and Capsida each have the option to co-develop and co-commercialize the program that the other leads.

Financial Overview

Since our inception in October 2013, we have devoted substantially all of our resources to our research and development efforts, identifying potential product candidates, undertaking drug discovery and preclinical development activities, building and protecting our intellectual property estate, 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, common share issuances, convertible loans and collaboration agreements with strategic partners.

While we were in a net income position in certain previous years due to upfront payments associated with our collaborations with Vertex, we have a history of recurring losses and expect to continue to incur losses for the foreseeable future. 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; conduct initial drug application supporting preclinical studies and initiate clinical trials for our product candidates; initiate preclinical testing and clinical trials for any other product candidates we identify and develop; maintain, expand and protect our intellectual property estate; further develop our gene editing platform; hire additional research, clinical and scientific personnel; incur facilities costs associated with such personnel growth; develop manufacturing infrastructure and conduct related regulatory validation activities; and incur additional costs associated with operating as a public company. Please refer to Part I, Item 2 of our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on February 15, 2022 for more information about these facilities.

Revenue Recognition

We have not generated any revenue to date from product sales and do not expect to do so in the near future. Revenue recognized for the three months ended March 31, 2022 and 2021 was not material. For additional information about our revenue recognition policy, see Note 2, "Summary of Significant Accounting Policies," in our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on February 15, 2022, as well as Note 7 of the notes to our unaudited condensed consolidated financial statements included in this Quarterly Report on Form 10-Q.

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 and clinical activities on our behalf;
- costs of purchasing lab supplies and non-capital equipment used in our preclinical activities and in manufacturing preclinical and clinical study materials;
- consultant fees;
- facility costs, including rent, depreciation and maintenance expenses; and
- fees and other payments related to 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 IND-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 or the subsequent commercialization of any product candidates we may successfully 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 collaborations with Vertex and ViaCyte, as well as in connection with the Bayer Transaction, we do not track research and development costs on a program-by-program basis.

Research and development activities are central to our business model. We expect our research and development costs to increase significantly for the foreseeable future as our current development programs progress, new programs are added and as we continue to prepare regulatory filings. These increases will likely include the costs related to the implementation and expansion of clinical trial sites and related patient enrollment, monitoring, program management and manufacturing expenses for current and future clinical trials.

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 pre-commercial expenses associated with our collaboration with Vertex, 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, and potential commercialization of our product candidates. In addition, we anticipate increased expenses related to the reimbursements of third-party patent related expenses in connection with certain of our in-licensed intellectual property.

Collaboration Expense, Net

Collaboration expense, net, consists of collaboration costs under our collaboration with Vertex.

Other Income (Expense), Net

Other income (expense), net consists primarily of interest income earned on investments.

Results of Operations

Comparison of three months ended March 31, 2022 and 2021 (in thousands):

	Three Months Ended March 31,		Period to Period Change
	2022	2021	
Revenue:			
Collaboration revenue	$ 178	$ 202	$ (24)
Grant revenue	762	337	425
Total revenue	940	539	401
Operating expenses:			
Research and development	118,245	70,620	47,625
General and administrative	28,021	24,517	3,504
Collaboration expense, net	30,646	19,945	10,701
Total operating expenses	176,912	115,082	61,830
Loss from operations	(175,972)	(114,543)	(61,429)
Other income, net	363	1,955	(1,592)
Net loss before income taxes	(175,609)	(112,588)	(63,021)
Provision for income taxes	(3,608)	(575)	(3,033)
Net loss	$ (179,217)	$ (113,163)	$ (66,054)

Collaboration Revenue

Collaboration revenue for the three months ended March 31, 2022 and 2021 was not material. Please refer to Note 7 of the notes to our unaudited condensed consolidated financial statements included in this Quarterly Report on Form 10-Q for further information.

Research and Development Expenses

Research and development expenses were $118.2 million for the three months ended March 31, 2022, compared to $70.6 million for the three months ended March 31, 2021. The increase of approximately $47.6 million was primarily attributable to the following:

- $24.6 million of increased variable research and development costs primarily associated with production of drug product and increased clinical trial expense associated with our oncology programs;
- $8.8 million of increased facility-related expenses, primarily related to our new U.S. research and development headquarters;
- $7.3 million of increased employee compensation, benefit and other headcount related expenses, of which $1.7 million is increased stock-based compensation expense, primarily due to an increase in headcount to support overall growth;
- $3.7 million of increased license fees; and
- $2.9 million of increased consulting and professional services costs.

General and Administrative Expenses

General and administrative expenses were $28.0 million for the three months ended March 31, 2022, compared to $24.5 million for the three months ended March 31, 2021. The increase of approximately $3.5 million was primarily attributable to the following:

- $2.2 million of increased employee compensation, primarily due to increased stock-based compensation expense of $1.9 million; and
- $1.3 million of increased consulting and professional services costs.

Collaboration Expense, Net

Collaboration expense, net, was $30.6 million for the three months ended March 31, 2022, compared to $19.9 million for the three months ended March 31, 2021. The increase of approximately $10.7 million was primarily attributable to the following:

- $6.5 million of increased pre-commercial expenses associated with our collaboration with Vertex;
- $5.3 million of increased manufacturing costs; offset by

- $1.3 million of decreased other costs.

Other Income, Net

Other income was $0.4 million for the three months ended March 31, 2022, compared to $2.0 million of income for the three months ended March 31, 2021. The change was primarily due to interest income earned on cash, cash equivalents and marketable securities for the three months ended March 31, 2022.

Liquidity and Capital Resources

As of March 31, 2022, we had cash, cash equivalents and marketable securities of approximately $2,221.3 million, of which approximately $395.7 million was held outside of the United States.

In August 2019, we entered into an Open Market Sale Agreement℠ with Jefferies LLC, or Jefferies, under which we are able to offer and sell, from time to time at our sole discretion through Jefferies, as our sales agent, our common shares, par value of CHF 0.03 per share, or the August 2019 Sales Agreement. In January 2021, in connection with the August 2019 Sales Agreement, we filed a prospectus supplement with the SEC to offer and sell from time to time common shares having aggregate gross proceeds of up to $600.0 million. In July 2021, we filed a new prospectus supplement with the SEC, which replaced the previous prospectus supplement filed in January 2021, to offer and sell, from time to time, common shares having aggregate gross proceeds of up to $419.8 million, or the 2021 ATM. No shares were issued and sold under the 2021 ATM for the three months ended March 31, 2022.

We have predominantly incurred losses and cumulative negative cash flows from operations since our inception. As of March 31, 2022, we had $2,221.3 million in cash, cash equivalents and marketable securities and an accumulated deficit of $375.1 million. We anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may raise through public or private equity or debt financings, strategic collaborations, or other sources.

Funding Requirements

Our primary uses of capital are, and we expect will continue to be, research and development activities, manufacturing activities, 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, including costs associated with operating as a public company. 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 and clinical activities and initiate preclinical studies to support initial drug applications. We also anticipate that we will incur significant capital expenditures as we develop our manufacturing infrastructure and facilities.

Because our research programs are still in early stages of development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development, manufacture and commercialization of any current or future product candidates, if approved, 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 financings, debt financings and payments received in connection with our collaboration agreements. We are eligible to earn payments, in each case, on a per-product basis under our collaboration with Vertex. Except for this source of funding, we do not have any committed external source of liquidity. We intend to consider opportunities to raise additional funds through the sale of equity or debt securities when market conditions are favorable to us to do so. However, the trading prices for our common shares and other biopharmaceutical companies have been highly volatile. As a result, we may face difficulties raising capital through sales of our common shares or such sales may be on unfavorable terms. In addition, a recession, depression or other sustained adverse market event, including resulting from the spread of the coronavirus, could materially and adversely affect our business and the value of our common shares. To the extent that we raise additional capital through the future sale of equity or debt securities, the ownership interests 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 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 with Vertex and any other capital raising transactions we may complete. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Given our need for additional financing to support the long-term clinical development of our programs, we intend to consider additional financing opportunities when market terms are favorable to us.

Our ability to generate revenue and achieve profitability depends significantly on our success in many areas, including: developing our delivery technologies and our gene-editing 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, if approved; 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 estate of intellectual property rights, including patents, trade secrets and know-how; and attracting, hiring and retaining qualified personnel.

Cash Flows

The following table provides information regarding our cash flows for each of the periods below (in thousands):

	Three Months Ended March 31,		Period to Period Change
	2022	2021	
Net cash used in operating activities	$ (135,239)	$ (100,663)	$ (34,576)
Net cash used in investing activities	(114,515)	(167,898)	53,383
Net cash provided by financing activities	10,649	225,991	(215,342)
Effect of exchange rate changes on cash	(27)	5	(32)
Net decrease in cash	$ (239,132)	$ (42,565)	$ (196,567)

Operating Activities

Net cash used in operating activities was $135.2 million for the three months ended March 31, 2022, compared to cash used in operating activities of $100.7 million for the three months ended March 31, 2021. The increase in cash used in operating activities of $34.5 million was primarily driven by an increase in net loss of $66.1 million, from a net loss of $113.2 million for the three months ended March 31, 2021 to net loss of $179.2 million for the three months ended March 31, 2022. The increase in cash used in operations was offset by an increase in non-cash expense of $11.0 million, primarily related to an increase in stock compensation, fixed asset depreciation and amortization of premiums and discounts on marketable securities, as well as a $20.5 million increase in net changes of operating assets and liabilities.

Investing Activities

Net cash used in investing activities for the three months ended March 31, 2022 was $114.5 million, compared to $167.9 million for the three months ended March 31, 2021. The decrease in net cash used in investing activities consisted primarily of a reduction in marketable securities maturities, offset by purchases of marketable securities and property and equipment.

Financing Activities

Net cash provided by financing activities for the three months ended March 31, 2022 was $10.6 million, compared with $226.0 million for the three months ended March 31, 2021. Net cash provided by financing activities for the three months ended March 31, 2022 consisted of option exercise proceeds, net of issuance costs. Net cash provided by financing activities for the three months ended March 31, 2021 consisted primarily of $222.1 million of net cash proceeds related to the issuance of 1.4 million common shares in connection with our 2021 ATM. No shares were issued and sold under the 2021 ATM for the three months ended March 31, 2022.

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. GAAP. 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.

We believe that our most critical accounting policies are those relating to revenue recognition, variable interest entities and equity-based compensation, and there have been no changes to our accounting policies discussed in our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on February 15, 2022.

Recent Accounting Pronouncements

Refer to Note 1 of the notes to our unaudited condensed consolidated financial statements included in this Quarterly Report on Form 10-Q for a discussion of recent accounting pronouncements.

Item 3. Qualitative and Quantitative Disclosures about Market Risk

Interest Rate Sensitivity

We are exposed to market risk related to changes in interest rates. As of March 31, 2022, we had cash, cash equivalents and marketable securities of $2,221.3 million, primarily invested in U.S. treasury securities and government agency securities, corporate bonds, commercial paper and money market accounts invested in U.S. government agency securities. Due to the conservative nature of these instruments, we do not believe that we have a material exposure to interest rate risk. If interest rates were to increase or decrease by 1%, the fair value of our investment portfolio would increase or decrease by an immaterial amount.

Foreign Currency Exchange Rate 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. Changes in foreign exchange rates affect our consolidated statement of operations and distort comparisons between periods. To date, foreign currency transaction gains and losses have not been material to our financial statements, and we have not engaged in any foreign currency hedging transactions.

Item 4. Controls and Procedures.

Management's Evaluation of our Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities and Exchange Act of 1934 is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure.

As of March 31, 2022, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities and Exchange Act of 1934). Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of March 31, 2022, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

During the quarter ended March 31, 2022, there were no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Securities Exchange Act of 1934, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

In the ordinary course of business, we are from time to time involved in lawsuits, investigations, proceedings and threats of litigation related to, among other things, our intellectual property estate (including certain in-licensed intellectual property), commercial arrangements and other matters. Such proceedings may include quasi-litigation, inter partes administrative proceedings in the U.S. Patent and Trademark Office and the European Patent Office involving our intellectual property estate including certain in-licensed intellectual property. 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.

There have been no material developments with respect to the legal proceedings previously disclosed in "Item 3. Legal Proceedings" of our Annual Report on Form 10-K for the fiscal year ended December 31, 2021 filed with the SEC on February 15, 2022.

Item 1A. Risk Factors.

In addition to the risks described in our Annual Report on Form 10-Kan, you should carefully consider the other information set forth in this Form 10-Q and the information in our other filings with the SEC, as they could materially affect our business, financial condition or future results of operations. There have been no material changes to the risk factors previously disclosed in Part I, Item 1A (Risk Factors) of our Annual Report on Form 10-K.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.

None.

Item 3. Defaults Upon Senior Securities.

Not applicable.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Other Information.

None.

Item 6. Exhibits

The exhibits filed as part of this Quarterly Report on Form 10-Q are set forth in the Exhibit Index below.

Exhibit Number	Description of Document
31.1*	Certification of Chief Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Chief Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1*+	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the inline XBRL document.
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.*)

* Filed herewith.

\+ The certification attached as Exhibit 32.1 that accompany this Quarterly Report on Form 10-Q are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of CRISPR Therapeutics AG under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-Q, irrespective of any general incorporation language contained in such filing.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

CRISPR Therapeutics AG

Dated: May 9, 2022

By: /s/ Samarth Kulkarni
Samarth Kulkarni
Chief Executive Officer
(Principal Executive Officer)

Dated: May 9, 2022

By: /s/ Brendan Smith
Brendan Smith
Chief Financial Officer
(Principal Financial Officer)

Exhibit 31.1

CERTIFICATIONS

I, Samarth Kulkarni, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of CRISPR Therapeutics AG;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 9, 2022

By: /s/ Samarth Kulkarni
Samarth Kulkarni
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Brendan Smith, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of CRISPR Therapeutics AG;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 9, 2022

By: /s/ Brendan Smith
Brendan Smith
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of CRISPR Therapeutics AG (the "Company") for the period ended March 31, 2022 as filed with the Securities and Exchange Commission on or about the date hereof (the "Report"), the undersigned officers of the Company hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to his or her knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company as of, and for, the periods presented in the Report.

/s/ Samarth Kulkarni
Samarth Kulkarni
Chief Executive Officer
(Principal Executive Officer)

May 9, 2022

/s/ Brendan Smith
Brendan Smith
Chief Financial Officer
(Principal Financial and Accounting Officer)

May 9, 2022