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 September 30, 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(s)	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 October 28, 2022, there were 78,294,139 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, "COBALT™," "CTX001™," "CTX110®," "CTX112™," "CTX120™," "CTX121™," "CTX130™," "CTX131™," "CRISPR TX™," "VCTX210™" and "VCTX211™," 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 exa-cel (formerly known as CTX001™), CTX110®, 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 exa-cel, CTX110, CTX112™, CTX130, VCTX210 and VCTX211™, 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 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	
	September 30, 2022	**December 31, 2021**
Assets		
Current assets:		
Cash and cash equivalents	$ 494,151	$ 923,031
Marketable securities	1,401,824	1,456,098
Accounts receivable	49	305
Prepaid expenses and other current assets	36,679	38,079
Total current assets	1,932,703	2,417,513
Property and equipment, net	166,110	137,575
Marketable securities, non-current	77,147	—
Intangible assets, net	84	125
Restricted cash	12,123	16,913
Operating lease assets	161,507	174,460
Other non-current assets	3,682	5,291
Total assets	$ 2,353,356	$ 2,751,877
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	$ 32,114	$ 14,816
Accrued expenses	102,954	91,003
Deferred revenue, current	—	1,011
Accrued tax liabilities	4,272	724
Operating lease liabilities	11,260	12,158
Other current liabilities	270	171
Total current liabilities	150,870	119,883
Deferred revenue, non-current	12,323	12,323
Operating lease liabilities, net of current portion	230,895	212,872
Other non-current liabilities	5,314	7,339
Total liabilities	399,402	352,417
Commitments and contingencies, see Note 6		
Shareholders' equity:		
Common shares, CHF 0.03 par value, 150,347,467 and 145,364,335 shares authorized at September 30, 2022 and December 31, 2021, respectively, 78,428,146 and 77,170,382 shares issued at September 30, 2022 and December 31, 2021, respectively, 78,247,830 and 76,990,066 shares outstanding at September 30, 2022 and December 31, 2021, respectively	2,433	2,391
Treasury shares, at cost, 180,316 shares at September 30, 2022 and at December 31, 2021	(63)	(63)
Additional paid-in capital	2,709,361	2,598,114
Accumulated deficit	(735,515)	(195,915)
Accumulated other comprehensive loss	(22,262)	(5,067)
Total shareholders' equity	1,953,954	2,399,460
Total liabilities and shareholders' equity	$ 2,353,356	$ 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) Income
(unaudited, in thousands, except share and per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Revenue:				
Collaboration revenue	$ 94	$ 329	$ 430	$ 900,733
Grant revenue	—	495	762	1,331
Total revenue	94	824	1,192	902,064
Operating expenses:				
Research and development	116,622	83,500	358,090	237,472
General and administrative	27,001	23,709	81,295	76,012
Collaboration expense, net	38,859	22,464	103,427	69,354
Total operating expenses	182,482	129,673	542,812	382,838
(Loss) income from operations	(182,388)	(128,849)	(541,620)	519,226
Other income:				
Other income, net	7,264	1,101	11,171	3,806
Total other income, net	7,264	1,101	11,171	3,806
Net (loss) income before income taxes	(175,124)	(127,748)	(530,449)	523,032
Benefit (provision) for income taxes	575	595	(9,151)	(4,123)
Net (loss) income	(174,549)	(127,153)	(539,600)	518,909
Foreign currency translation adjustment	(100)	(24)	(195)	(14)
Unrealized loss on marketable securities	(1,820)	(117)	(17,001)	(673)
Comprehensive (loss) income	$ (176,469)	$ (127,294)	$ (556,796)	$ 518,222
Net (loss) income per common share — basic	$ (2.24)	$ (1.67)	$ (6.96)	$ 6.85
Basic weighted-average common shares outstanding	78,021,520	76,288,534	77,547,771	75,712,437
Net (loss) income per common share — diluted	$ (2.24)	$ (1.67)	$ (6.96)	$ 6.44
Diluted weighted-average common shares outstanding	78,021,520	76,288,534	77,547,771	80,554,682

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
Vesting of restricted shares	3,667	—	—	—	—	—	—	—
Exercise of vested options, net of issuance costs of $0.4 million	344,158	12	—	—	10,897	—	—	10,909
Stock-based compensation expense	—	—	—	—	28,331	—	—	28,331
Other comprehensive loss	—	—	—	—	—	—	(168)	(168)
Net income	—	—	—	—	—	759,225	—	759,225
Balance at June 30, 2021	76,078,453	$ 2,352	195,316	$ (63)	$ 2,529,649	$ 72,486	$ (629)	$ 2,603,795
Vesting of restricted shares	96,167	4	—	—	—	—	—	4
Exercise of vested options, net of issuance costs of $0.4 million	278,227	10	(15,000)	—	8,865	—	—	8,875
Purchase of common stock under ESPP	10,333	—	—	—	1,344	—	—	1,344
Stock-based compensation expense	—	—	—	—	26,199	—	—	26,199
Other comprehensive loss	—	—	—	—	—	—	(141)	(141)
Net loss	—	—	—	—	—	(127,153)	—	(127,153)
Balance at September 30, 2021	76,463,180	$ 2,366	180,316	$ (63)	$ 2,566,057	$ (54,667)	$ (770)	$ 2,512,923
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
Vesting of restricted shares	14,705	—	—	—	—	—	—	—
Exercise of vested options, net of issuance costs of $0.2 million	391,053	13	—	—	10,333	—	—	10,346
Stock-based compensation expense	—	—	—	—	24,852	—	—	24,852
Other comprehensive loss	—	—	—	—	—	—	(3,449)	(3,449)
Net loss	—	—	—	—	—	(185,834)	—	(185,834)
Balance at June 30, 2022	77,792,163	$ 2,420	180,316	$ (63)	$ 2,669,782	$ (560,966)	$ (20,342)	$ 2,090,831
Issuance of common shares	12,365	—	—	—	970	—	—	970
Vesting of restricted shares	17,128	1	—	—	—	—	—	1
Exercise of vested options, net of issuance costs of $0.3 million	401,110	12	—	—	12,770	—	—	12,782
Purchase of common stock under ESPP	25,064	—	—	—	1,296	—	—	1,296
Stock-based compensation expense	—	—	—	—	24,543	—	—	24,543
Other comprehensive loss	—	—	—	—	—	—	(1,920)	(1,920)
Net loss	—	—	—	—	—	(174,549)	—	(174,549)
Balance at September 30, 2022	78,247,830	$ 2,433	180,316	$ (63)	$ 2,709,361	$ (735,515)	$ (22,262)	$ 1,953,954

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)

	Nine Months Ended September 30,	
	2022	2021
Operating activities:		
Net (loss) income	$ (539,600)	$ 518,909
Reconciliation of net (loss) income to net cash used in operating activities:		
Depreciation and amortization	18,326	11,692
Equity-based compensation	75,142	76,622
Other non-cash items, net	12,251	9,420
Changes in:		
Accounts receivable	256	(8)
Prepaid expenses and other assets	7,062	(18,775)
Accounts payable and accrued expenses	36,261	14,733
Deferred revenue	(762)	(779)
Operating lease assets and liabilities	10,826	19,679
Other liabilities, net	(2,175)	(6,483)
Net cash (used in) provided by operating activities	(382,413)	625,010
Investing activities:		
Purchase of property, plant and equipment	(30,997)	(72,522)
Purchases of marketable securities	(923,404)	(1,386,785)
Maturities of marketable securities	871,278	432,593
Net cash used in investing activities	(83,123)	(1,026,714)
Financing activities:		
Proceeds from issuance of common shares, net of issuance costs	970	213,267
Proceeds from exercise of options and ESPP contributions, net of issuance costs	35,144	31,379
Net cash provided by financing activities	36,114	244,646
Effect of exchange rate changes on cash	(195)	(14)
Decrease in cash	(429,617)	(157,072)
Cash, cash equivalents and restricted cash, beginning of period	939,944	1,185,468
Cash, cash equivalents and restricted cash, end of period	$ 510,327	$ 1,028,396
Supplemental disclosure of non-cash investing and financing activities		
Property and equipment purchases in accounts payable and accrued expenses	$ 4,919	$ 6,264
Equity issuance costs in accounts payable and accrued expenses	$ 299	$ 391
Leasehold improvements paid directly by landlord	$ 19,252	$ —

	As of September 30,	
Reconciliation to amounts within the condensed consolidated balance sheets	2022	2021
Cash and cash equivalents	494,151	1,011,548
Prepaid expenses and other current assets	4,053	—
Restricted cash	12,123	16,848
Cash, cash equivalents and restricted cash at end of period	$ 510,327	$ 1,028,396

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 and nine-month interim periods ended September 30, 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) income. As a result, collaboration costs under the Vertex Agreements accounted for under ASC 808 for the three and nine months ended September 30, 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 and nine months ended September 30, 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 September 30, 2022 and December 31, 2021 (in thousands), which are recorded at fair value. The table below excludes $279.9 million and $405.6 million of cash at September 30, 2022 and December 31, 2021, respectively.

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
September 30, 2022				
Cash equivalents:				
Money market funds	$ 37,857	$ —	$ —	$ 37,857
Corporate debt securities	20,232	2	(14)	20,220
Certificates of deposit	14,481	—	—	14,481
Commercial paper	141,727	—	(11)	141,716
Total cash equivalents	214,297	2	(25)	214,274
Marketable securities:				
U.S. Treasury securities	46,340	—	(15)	46,325
Corporate debt securities	1,102,619	18	(20,742)	1,081,895
Certificates of deposit	44,430	—	—	44,430
Government-sponsored enterprise securities	43,053	21	(627)	42,447
Commercial paper	264,610	—	(736)	263,874
Total marketable securities	1,501,052	39	(22,120)	1,478,971
Total cash equivalents and marketable securities	$ 1,715,349	$ 41	$ (22,145)	$ 1,693,245
December 31, 2021				
Cash equivalents:				
Money market funds	$ 507,386	$ —	$ —	$ 507,386
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 September 30, 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 $814.9 million and $1,311.6 million, respectively. As of September 30, 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 $506.2 million and $4.6 million, respectively. Of this amount, securities totaling $77.1 million and $0.0 million as of September 30, 2022 and December 31, 2021, respectively, will mature beyond one year. The Company has recorded a net unrealized loss of $1.8 million and $17.0 million during the three and nine months ended September 30, 2022 respectively, related to its debt securities, which is included in comprehensive loss on the condensed consolidated statements of operations and comprehensive (loss) income. The Company recorded a net unrealized loss of $0.1 million and $0.7 million during the three and nine months ended September 30, 2021 respectively, related to its debt securities, which is included in comprehensive loss on the condensed consolidated statements of operations and comprehensive (loss) income.

The Company determined that there is no material credit risk associated with the above investments as of September 30, 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 and nine months ended September 30, 2022 and 2021. No available-for-sale debt securities held as of September 30, 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 September 30, 2022 and December 31, 2021 (in thousands):

	Fair Value Measurements at September 30, 2022			
	Total	Level 1	Level 2	Level 3
Cash and cash equivalents:				
Cash	$ 279,877	$ 279,877	$ —	$ —
Money market funds	37,857	37,857	—	—
Corporate debt securities	20,220	—	20,220	—
Commercial paper	141,716	—	141,716	—
Certificates of deposit	14,481	—	14,481	—
Marketable securities:				
U.S. Treasury securities	46,325	—	46,325	—
Corporate debt securities	1,081,895	—	1,081,895	—
Certificates of deposit	44,430	—	44,430	—
Government-sponsored enterprise securities	42,447	—	42,447	—
Commercial paper	263,874	—	263,874	—
Other non-current assets	2,212	—	—	2,212
Total	$ 1,975,334	$ 317,734	$ 1,655,388	$ 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	—	—
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	
	September 30, 2022	December 31, 2021
Computer equipment	$ 3,479	$ 1,757
Furniture, fixtures and other	7,850	4,371
Laboratory equipment	36,231	30,123
Leasehold improvements	141,914	86,735
Construction work in process	4,604	52,396
Total property and equipment, gross	194,078	175,382
Accumulated depreciation	(27,968)	(37,807)
Total property and equipment, net	$ 166,110	$ 137,575

Depreciation expense for the three and nine months ended September 30, 2022 was $5.0 million and $18.3 million, respectively. Depreciation expense for the three and nine months ended September 30, 2021 was $5.3 million and $11.7 million, respectively.

5. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	As of	
	September 30, 2022	December 31, 2021
Payroll and employee-related costs	$ 18,906	$ 23,661
Research costs	69,485	47,986
Licensing fees	1,239	138
Professional fees	4,834	4,720
Intellectual property costs	3,790	6,120
Accrued property and equipment	3,966	7,113
Other	734	1,265
Total	$ 102,954	$ 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 September 30, 2022, the Company had restricted cash of $16.2 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 $4.1 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 September 30, 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 its own cost in certain defined areas that, if beneficial to the exagamglogene autotemcel, or exa-cel, program (formerly known as 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 exa-cel 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 September 30, 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 exa-cel program prospectively; (b) adjust the allocation of net profits and net losses between the parties with respect to exa-cel 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 exa-cel) 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 exa-cel 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., exa-cel) 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 exa-cel program exceeds specified amounts. Any deferred amounts are only payable to Vertex as an offset against future profitability of the exa-cel 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 exa-cel program exceeds specified amounts, which are only payable to Vertex as an offset against future profitability of the exa-cel 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 exa-cel program and the right to control development and commercialization of exa-cel, or the "Exa-cel Exclusive License." The Company concluded the Exa-cel Exclusive License was both capable of being distinct and distinct within the context of the A&R Vertex JDCA, and the Exa-cel Exclusive License was sold at its estimated standalone selling price, or "ESSP." As such, the Exa-cel 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 Exa-cel 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 Exa-cel 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 exa-cel 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 Exa-cel Exclusive License was the only performance obligation, the entire transaction price was allocated to the Exa-cel 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 Exa-cel 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 Exa-cel 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 and nine months ended September 30, 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 September 30, 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 and nine months ended September 30, 2022, respectively, was not material. Revenue recognized under the Vertex Agreements for the three and nine months ended September 30, 2021, respectively, was $0.2 million and $900.6 million, respectively.

As of September 30, 2022 and December 31, 2021, there was no current deferred revenue related to the collaboration with Vertex. As of September 30, 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 exa-cel program and exa-cel 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 September 30, 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 exa-cel 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) income.

During the three and nine months ended September 30, 2022, the Company recognized $38.9 million and $103.4 million of collaboration expense, net, related to the Vertex Agreements, respectively. Collaboration expense, net, was net of $10.1 million and $26.6 million of reimbursements from Vertex, respectively. During the three and nine months ended September 30, 2021, the Company recognized $22.5 million and $69.4 million of collaboration expense, net, related to the Vertex Agreements, respectively. Collaboration expense, net, was net of $15.8 million and $39.0 million of reimbursements from Vertex, respectively.

8. Share Capital

The Company had 150,347,467 authorized common shares as of September 30, 2022, with a par value of CHF 0.03 per share. Share Capital consisted of the following:

Type of Share Capital	Conditional Capital	As of September 30, 2022	As of 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	8,202,832	4,919,700
Common shares	Conditional share capital - Employee benefit plans	20,799,332	20,806,433
	Total	150,347,467	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, the common shares remaining under the original prospectus supplement having aggregate gross proceeds of up to $419.8 million, or, together with the January 2021 prospectus supplement, the 2021 ATM.

As of September 30, 2022, the Company has issued and sold an aggregate of 1.1 million common shares under the 2021 ATM at an average price of $168.79 per share for aggregate proceeds of $178.8 million, which were net of equity issuance costs of $2.4 million.

9. Stock-based Compensation

During the three and nine months ended September 30, 2022 and 2021, the Company recognized the following stock-based compensation expense (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Research and development	$ 13,311	$ 14,190	$ 41,728	$ 43,230
General and administrative	11,232	12,009	33,414	33,392
Total	$ 24,543	$ 26,199	$ 75,142	$ 76,622

Stock option activity

The following table summarizes stock option activity for the nine months ended September 30, 2022:

	Shares	Weighted-average exercise price per share
Outstanding at December 31, 2021	7,812,982	$ 58.07
Granted	1,143,989	59.84
Exercised	(1,053,443)	32.17
Cancelled or forfeited	(649,697)	82.40
Outstanding at September 30, 2022	7,253,831	$ 59.93
Exercisable at September 30, 2022	4,637,194	$ 49.37
Vested and expected to vest at September 30, 2022	7,253,831	$ 59.93

As of September 30, 2022, total unrecognized compensation expense related to stock options was $121.4 million, which the Company expects to recognize over a remaining weighted-average period of 2.4 years.

Restricted stock activity

The following table summarizes restricted stock activity for the nine months ended September 30, 2022:

	Restricted Stock	Weighted-Average Grant Date Fair Value
Unvested balance as of December 31, 2021	934,175	$ 100.14
Granted	714,376	65.66
Vested	(155,397)	86.15
Cancelled or forfeited	(171,978)	92.45
Unvested balance as of September 30, 2022	1,321,176	$ 84.14

As of September 30, 2022, total unrecognized compensation expense related to unvested restricted common shares was $78.4 million, which the Company expects to recognize over a remaining weighted-average vesting period of 2.5 years.

During the third quarter of 2022, the Company granted 150,000 performance stock units with market-based vesting conditions in which the recipient is eligible to receive between zero and 150,000 common shares at the end of a three-year service period based upon achieving a specified average stock price. The expense for these awards is being recognized over the requisite service period. As of September 30, 2022, 150,000 of the performance stock units were unvested.

10. Net (Loss) Income Per Share Attributable to Common Shareholders

Basic net (loss) income per share is calculated by dividing net (loss) income attributable to common shareholders by the weighted-average number of common shares outstanding during the period. Diluted net (loss) income per share is calculated by dividing the net (loss) income 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) income is net (loss) income attributable to common shareholders for all periods presented.

The following table sets forth the computation of basic and diluted net (loss) income per share for the periods indicated (in thousands, except for share and per share amounts):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Net (loss) income	$ (174,549)	$ (127,153)	$ (539,600)	$ 518,909
Basic weighted-average common shares outstanding	78,021,520	76,288,534	77,547,771	75,712,437
Effect of potentially dilutive securities:				
Outstanding options	—	—	—	4,340,103
Unvested restricted common shares	—	—	—	502,142
Diluted weighted-average common shares outstanding	78,021,520	76,288,534	77,547,771	80,554,682
Basic net (loss) income per common share	(2.24)	(1.67)	(6.96)	6.85
Diluted net (loss) income per common share	(2.24)	(1.67)	(6.96)	6.44

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Outstanding options	7,253,831	7,887,772	7,253,831	1,556,588
Unvested restricted common shares	1,321,176	1,016,231	1,321,176	143,617
ESPP	8,673	7,685	8,673	6,578
Total	8,583,680	8,911,688	8,583,680	1,706,783

11. Income Taxes

During the three and nine months ended September 30, 2022, the Company recorded an income tax benefit of $0.6 million and an income tax provision of $9.2 million, respectively, representing an effective tax rate of 0.3% and (1.7%), respectively. During the three and nine months ended September 30, 2021, the Company recorded an income tax benefit of $0.6 million and an income tax provision of $4.1 million, respectively, representing an effective tax rate of 0.5% and 0.8%, respectively. The income tax benefit for the three months ended September 30, 2022 and the income tax provision for the nine months ended September 30, 2022 are primarily attributable to the Company's U.S. subsidiaries. The decrease in the rate for the three and nine months ended September 30, 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. Additionally, the Company was profitable for the nine months ended September 30, 2021 but is in a loss position for nine months ended September 30, 2022 which causes the tax rate to be negative in the current period. 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.

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. Dr. Charpentier and 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. We believe that our scientific expertise, together with our gene-editing approach, may enable an entirely new class of highly active and potentially curative therapies for patients, including those for whom current biopharmaceutical approaches have had limited success.

We have established a portfolio of therapeutic programs in a broad range of disease areas across four core franchises: hemoglobinopathies, oncology, regenerative medicine and *in vivo* approaches.

Hemoglobinopathies

Our lead product candidate, CTX001, now known as exagamglogene autotemcel, or exa-cel, 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. Exa-cel 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 exa-cel in two ongoing Phase 3 open-label clinical trials that are designed to assess the safety and efficacy of a single dose of exa-cel in patients ages 12 to 35 with TDT (CLIMB-111) or SCD (CLIMB-121), respectively. Enrollment is complete for both CLIMB-111 and CLIMB-121. We and Vertex have also initiated two additional Phase 3 open-label clinical trials of exa-cel in pediatric patients with TDT (CLIMB-141) and SCD (CLIMB-151). Patients who received exa-cel in CLIMB-111, CLIMB-121, CLIMB-141 or CLIMB-151 will be asked to participate in a long-term, open-label follow-up trial, CLIMB-131, to evaluate the safety and efficacy of exa-cel. CLIMB-131 is designed to follow participants for up to 15 years after exa-cel infusion. In the second quarter of 2022, at the European Hematology Association Congress, we presented updated clinical data from CLIMB-111 and CLIMB-121 for 44 patients with TDT and 31 patients with SCD treated with exa-cel. Exa-cel has been granted a number of regulatory designations from the U.S. Food and Drug Administration, or FDA, including RMAT, Fast Track, Orphan Drug, and Rare Pediatric Disease designations for the treatment of both TDT and SCD. Exa-cel 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. In the third quarter of 2022, we and Vertex announced that discussions with the FDA have concluded, and the FDA granted exa-cel a rolling review for the potential treatment of SCD and TDT. The exa-cel biologics licensing application will be submitted for rolling review, beginning in November 2022 and the parties expect the submission to be complete by the end of the first quarter of 2023. Discussions were previously completed with the European Medicines Agency and the Medicines and Healthcare products Regulatory Agency on the data required to support marketing applications for exa-cel and such applications are on track for submission by the end of 2022.

In addition, building upon exa-cel, we have next-generation efforts in targeted conditioning and *in vivo* editing of hematopoietic stem cells, either of which could broaden the number of patients that can benefit from our therapies.

Immuno-Oncology

We are developing a portfolio of wholly-owned 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.

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 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 in adult patients. The COBALT™-LYM trial is evaluating the safety and efficacy of CTX130 for the treatment of relapsed or refractory T or B cell malignancies. The COBALT-RCC trial is evaluating the safety and efficacy of CTX130 for the treatment of relapsed or refractory renal cell carcinoma. CTX130 has received Orphan Drug Designation from the FDA for the treatment of T cell lymphoma and RMAT designation for the treatment of Mycosis Fungoides and Sézary Syndrome (MF/SS). In the second quarter of 2022, at the European Hematology Association Congress, we released initial clinical data from the ongoing COBALT-LYM trial for 18 patients with T cell lymphoma treated with CTX130 who had reached at least 28 days of follow-up. Also in the second quarter of 2022, we released preliminary clinical data from the COBALT-RCC trial for 14 patients.

Next-generation candidates

Our CRISPR/Cas9 platform enables us to innovate continuously by incorporating incremental edits into next-generation products. We are advancing multiple next-generation CAR-T product candidates, including CTX112 targeting CD19 and CTX131™ targeting CD70, which incorporate additional edits designed to enhance CAR-T potency; and in the third quarter of 2022, the Investigational New Drug Application for CTX112 was cleared by the FDA. In addition, as we previously disclosed, following our June 2022 disclosure of high-level data from our Phase 1 clinical trial investigating CTX120™, a healthy donor-derived gene-edited allogeneic CAR-T investigational therapy targeting B-cell maturation antigen, or BCMA, for the treatment of relapsed or refractory multiple myeloma, we announced plans to pivot to a next-generation allogeneic CAR-T targeting BCMA, CTX121™, which incorporates proprietary edits to enhance the potency of the CAR-T cells.

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 allogeneic stem cell-derived therapies using CRISPR/Cas9 gene editing to enable immune evasion, improve cell function, and direct cell fate. Our first major effort in this area is in diabetes, and we and ViaCyte, Inc., or ViaCyte, are advancing a series of programs as part of a strategic collaboration for the discovery, development, and commercialization of gene-edited stem cell therapies for the treatment of diabetes.

We have a multi-staged product strategy that leverages our CRISPR/Cas9 platform to advance multiple product candidates incorporating incremental edits designed to increase benefit. Our initial product candidate, 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. VCTX210 has gene edits designed to promote immune evasion and cell fitness. 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. Our next product candidate, VCTX211, an allogeneic, gene-edited, stem cell-derived product candidate for the treatment of T1D, incorporates additional gene edits that aim to further enhance cell fitness. In the third quarter of 2022, the Clinical Trial Application for VCTX211 was cleared by Health Canada.

In Vivo

Our *in vivo* gene editing strategy focuses on gene disruption and whole gene correction – the two technologies required to address ~90% of the most prevalent severe monogenic diseases. We have established a leading platform for *in vivo* gene disruption, starting in the liver. We plan to advance a broad portfolio of programs across both rare and common diseases with this platform, starting with cardiovascular diseases. Gene editing has the potential to shift the treatment paradigm for cardiovascular diseases by recapitulating the proven benefit of natural human genetic variants in a single-dose format. In addition, we continue to develop an expansive whole gene correction platform, starting with lipid nanoparticles, or LNP, plus adeno-associated viral vectors, or AAV, in the liver and advancing to AAV-free, HDR-independent methodologies.

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 exa-cel 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 exa-cel 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, or the ViaCyte JDCA. In connection with entering into the ViaCyte JDCA, our existing research collaboration agreement with ViaCyte expired in accordance with its terms. Under the ViaCyte JDCA, we and ViaCyte are jointly developing and will commercialize product candidates and shared products for use in the treatment of diabetes type 1, diabetes type 2 and insulin dependent/requiring diabetes, or the ViaCyte Collaboration Field, throughout the world. The ViaCyte JDCA includes, among other things, provisions relating to collaboration and program governance, clinical activities for the product candidates and shared products under the agreement and continuing research by the parties in the ViaCyte Collaboration Field. Unless otherwise mutually agreed, research costs incurred by a party will be solely borne by such party. The program expenses, as originally set forth in the research and collaboration agreement, as applicable, incurred through the date of first commercial sale of a shared product will be allocated 60% to us and 40% to ViaCyte. Following first commercial sale of a shared product, such program expenses will be shared equally between us and ViaCyte. Shared product revenues will be shared equally by us and ViaCyte. In the third quarter of 2022, Vertex announced it had acquired ViaCyte.

Bayer. We entered into an option agreement in the fourth quarter of 2019 with Bayer pursuant to which Bayer has an option to co-develop and co-commercialize two products that we advance 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.

Other Partnerships. We have entered into a number of additional collaborations and license agreements to support and complement our hematopoietic stem cell, immuno-oncology, regenerative medicine and *in vivo* programs and platform, including agreements with: Nkarta, Inc. to co-develop and co-commercialize two donor-derived, gene-edited CAR-NK cell product candidates and a product candidate combining NK and T cells; Capsida Biotherapeutics, Inc. to develop *in vivo* gene editing therapies delivered with engineered AAV vectors for the treatment of amyotrophic lateral sclerosis and Friedreich's ataxia; Moffitt Cancer Center and Roswell Park Comprehensive Cancer Center to advance autologous CAR-T programs against new targets; MaxCyte, Inc. on *ex vivo* delivery for our hemoglobinopathy and immuno-oncology programs; CureVac AG on optimized mRNA constructs and manufacturing for certain *in vivo* programs; and KSQ Therapeutics, Inc. on intellectual property for our allogeneic immuno-oncology programs.

Special Note About Coronavirus (COVID-19)

The ongoing COVID-19 pandemic continues to have unpredictable impacts on global societies, economies, financial markets, and business practices around the world. The extent and duration of such effects remain uncertain and difficult to predict, particularly as virus variants continue to spread. We are actively monitoring and managing our response and evaluating the actual and potential impacts to our business operations, including on our ongoing and planned clinical trials. We will continue to work closely with our third-party vendors, collaborators, and other parties in order to seek to advance our programs and pipeline of product candidates, while keeping the health and safety of our employees and their families, partners, third-party vendors, healthcare providers, patients and communities a top priority. Please refer to our Risk Factors in Part II, Item IA of our Annual Report on Form 10-K for further discussion of risks related to the COVID-19 pandemic.

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 certain 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, defend, protect and expand 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.

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 and nine months ended September 30, 2022 was not material. Revenue recognized for the three and nine months ended September 30, 2021 was $0.8 million and $902.1 million, respectively. 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.

Our external research and development expenses support our various preclinical and clinical programs, and as such we do not break down external research and development expenses further. Our internal research and development expenses consist of payroll and benefits expenses, facilities expense, and other indirect research and development expenses incurred in support of overall research and development activities and as such are not allocated to a specific development stage or therapeutic area. 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.

Research and development activities are central to our business model. We expect to continue to incur research and development costs consistent with research and development at companies of our size and stage of development, which may increase in the foreseeable future as our current development programs progress, new programs are added and 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 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 expect to continue to incur general and administrative expenses consistent with research and development at companies of our size and stage of development, which may increase in the future to support continued research and development activities, and potential commercialization of our product candidates. In addition, we anticipate ongoing expenses related to the reimbursements of third-party patent related expenses in connection with certain of our in-licensed intellectual property, including related to the appeal of the U.S. Patent and Trademark Office's Patent and Trial Appeal Board's February 2022 Decision of Priority and Judgment in an interference declared in June 2019 between Dr. Emmanuelle Charpentier, the University of Vienna and the Regents of the University of California, or collectively, the CVC Group, and the Broad Institute, Massachusetts Institute of Technology and, in some instances, the President and Fellows of Harvard College, or collectively, the Broad, finding that Broad has priority over CVC Group with respect to the subject matter of the interference.

Collaboration Expense, Net

Collaboration expense, net, consists of operating expenses under our collaboration with Vertex. We will continue to incur operating expenses under our collaboration with Vertex in 2022. However, we anticipate that our operating expenses will exceed the specified maximum amount per year set forth in the A&R Vertex JDCA before year end, at which time we may defer a portion of our share of current year operating expenses on the exa-cel program 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 September 30, 2022 and 2021 (in thousands):

	Three Months Ended September 30,		Period to Period
	2022	2021	Change
Revenue:			
Collaboration revenue	$ 94	$ 329	$ (235)
Grant revenue	—	495	(495)
Total revenue	94	824	(730)
Operating expenses:			
Research and development	116,622	83,500	33,122
General and administrative	27,001	23,709	3,292
Collaboration expense, net	38,859	22,464	16,395
Total operating expenses	182,482	129,673	52,809
Loss from operations	(182,388)	(128,849)	(53,539)
Other income, net	7,264	1,101	6,163
Loss before income taxes	(175,124)	(127,748)	(47,376)
Benefit for income taxes	575	595	(20)
Net loss	$ (174,549)	$ (127,153)	$ (47,396)

Collaboration Revenue

Collaboration revenue for the three months ended September 30, 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 $116.6 million for the three months ended September 30, 2022, compared to $83.5 million for the three months ended September 30, 2021. The following table summarizes our research and development expenses for the three months ended September 30, 2022 and 2021, together with the changes in those items in dollars (in thousands):

	Three Months Ended September 30,		Period to Period
	2022	2021	Change
External research and development expenses	$ 51,243	$ 26,729	$ 24,514
Employee related expenses	21,122	8,866	12,256
Facility expenses	27,203	28,283	(1,080)
Stock-based compensation expenses	13,311	14,190	(879)
Other expenses	860	470	390
Sublicense and license fees	2,883	4,962	(2,079)
Total research and development expenses	$ 116,622	$ 83,500	$ 33,122

The increase of approximately $33.1 million was primarily attributable to the following:

- $24.5 million of increased external research and development costs, primarily associated with production of drug product and increased clinical trial expense associated with our oncology programs; and
- $12.3 million of increased employee-related expenses primarily due to an increase in headcount to support overall growth; offset by
- $2.1 million of decreased sublicense and license fees.

General and Administrative Expenses

General and administrative expenses were $27.0 million for the three months ended September 30, 2022, compared to general and administrative expenses of $23.7 million for the three months ended September 30, 2021. The increase in general and administrative expenses of $3.3 million was primarily attributable to increased employee-related expenses.

Collaboration Expense, Net

Collaboration expense, net, was $38.9 million for the three months ended September 30, 2022, compared to $22.5 million for the three months ended September 30, 2021. The increase of approximately $16.4 million was primarily attributable to increased manufacturing and other pre-commercial costs.

Other Income, Net

Other income was $7.3 million for the three months ended September 30, 2022, compared to $1.1 million of income for the three months ended September 30, 2021. The change was primarily due to interest income earned on cash, cash equivalents and marketable securities for the three months ended September 30, 2022.

Comparison of nine months ended September 30, 2022 and 2021 (in thousands):

	Nine Months Ended September 30,		Period to Period Change
	2022	2021	
Revenue:			
Collaboration revenue	$ 430	$ 900,733	$ (900,303)
Grant revenue	762	1,331	(569)
Total revenue	1,192	902,064	(900,872)
Operating expenses:			
Research and development	358,090	237,472	120,618
General and administrative	81,295	76,012	5,283
Collaboration expense, net	103,427	69,354	34,073
Total operating expenses	542,812	382,838	159,974
(Loss) income from operations	(541,620)	519,226	(1,060,846)
Other income, net	11,171	3,806	7,365
Net (loss) income before income taxes	(530,449)	523,032	(1,053,481)
Provision for income taxes	(9,151)	(4,123)	(5,028)
Net (loss) income	$ (539,600)	$ 518,909	$ (1,058,509)

Collaboration Revenue

Collaboration revenue for the nine months ended September 30, 2022 was not material. Collaboration revenue for the nine months ended September 30, 2021 was $900.7 million which was primarily associated with the $900.0 million upfront payment from Vertex in connection with the A&R Vertex JDCA. 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 $358.1 million for the nine months ended September 30, 2022, compared to $237.5 million for the nine months ended September 30, 2021. The following table summarizes our research and development expenses for the nine months ended September 30, 2022 and 2021, together with the changes in those items in dollars (in thousands):

	Nine Months Ended September 30,		Period to Period
	2022	2021	Change
External research and development expenses	$ 152,850	$ 79,041	$ 73,809
Employee related expenses	63,994	35,177	28,817
Facility expenses	87,981	72,045	15,936
Stock-based compensation expenses	41,728	43,230	(1,502)
Other expenses	2,112	1,372	740
Sublicense and license fees	9,425	6,607	2,818
Total research and development expenses	$ 358,090	$ 237,472	$ 120,618

The increase of approximately $120.6 million was primarily attributable to the following:

- $73.8 million of increased external research and development costs, primarily associated with production of drug product and increased clinical trial expense associated with our oncology programs;
- $28.8 million of increased employee-related expenses primarily due to an increase in headcount to support overall growth; and
- $15.9 million of increased facility-related expenses, primarily related to our new U.S. research and development headquarters located in Boston, Massachusetts.

General and Administrative Expenses

General and administrative expenses were $81.3 million for the nine months ended September 30, 2022, compared to $76.0 million for the nine months ended September 30, 2021. The increase of approximately $5.3 million was primarily attributable to increased employee-related expenses.

Collaboration Expense, Net

Collaboration expense, net, was $103.4 million for the nine months ended September 30, 2022, compared to $69.4 million for the nine months ended September 30, 2021. The increase of approximately $34.0 million was primarily attributable to the following:

- $19.7 million of increased manufacturing costs;
- $9.6 million of increased pre-commercial expenses associated with our collaboration with Vertex; and
- $4.7 million of increased other costs.

Other Income, Net

Other income was $11.2 million for the nine months ended September 30, 2022, compared to $3.8 million of income for the nine months ended September 30, 2021. The change was primarily due to interest income earned on cash, cash equivalents and marketable securities for the nine months ended September 30, 2022.

Liquidity and Capital Resources

As of September 30, 2022, we had cash, cash equivalents and marketable securities of approximately $1,973.1 million, of which approximately $29.2 million was held outside of the United States.

In August 2019, we entered into an Open Market Sale Agreement[SM] 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, the common shares remaining under the original prospectus supplement having aggregate gross proceeds of up to $419.8 million, or, together with the January 2021 prospectus supplement, the 2021 ATM. As of September 30, 2022, we have issued and sold an aggregate of 1.1 million common shares under the 2021 ATM at an average price of $168.79 per share for aggregate proceeds of $178.8 million, which were net of equity issuance costs of $2.4 million.

We have predominantly incurred losses and cumulative negative cash flows from operations since our inception. As of September 30, 2022, we had $1,973.1 million in cash, cash equivalents and marketable securities and an accumulated deficit of $735.5 million. We anticipate that we will continue to incur losses for at least the next several years. We expect to continue to incur research and development costs and general and administrative expenses consistent with research and development at companies of our size and stage of development, 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, defense and intellectual property maintenance costs, and general overhead costs, including costs associated with operating as a public company. We expect to continue to incur operating expenses consistent with research and development at companies of our size and stage of development, which may increase in the future to support continued research and development activities, and potential commercialization of our product candidates.

Because most of our 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 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 continued 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, defending, 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):

	Nine Months Ended September 30,		Period to Period
	2022	2021	Change
Net cash (used in) provided by operating activities	$ (382,413)	$ 625,010	$ (1,007,423)
Net cash used in investing activities	(83,123)	(1,026,714)	943,591
Net cash provided by financing activities	36,114	244,646	(208,532)
Effect of exchange rate changes on cash	(195)	(14)	(181)
Net decrease in cash	$ (429,617)	$ (157,072)	$ (272,545)

Operating Activities

Net cash used in operating activities was $382.4 million for the nine months ended September 30, 2022, compared to cash provided by operating activities of $625.0 million for the nine months ended September 30, 2021. The increase in cash used in operating activities of $1,007.4 million was primarily driven by an increase in net loss of $1,058.5 million, from net income of $518.9 million for the nine months ended September 30, 2021 to net loss of $539.6 million for the nine months ended September 30, 2022. The increase in cash used in operations was offset by an increase in non-cash expense of $8.0 million, primarily related to an increase in fixed asset depreciation and amortization of premiums and discounts on marketable securities, as well as a $43.1 million increase in net changes of operating assets and liabilities.

Investing Activities

Net cash used in investing activities for the nine months ended September 30, 2022 was $83.1 million, compared to $1,026.7 million for the nine months ended September 30, 2021. The decrease in net cash used in investing activities consisted primarily of an increase in marketable securities maturities, in addition to a reduction of purchases of marketable securities and property and equipment.

Financing Activities

Net cash provided by financing activities for the nine months ended September 30, 2022 was $36.1 million, compared with $244.6 million for the nine months ended September 30, 2021. Net cash provided by financing activities for the nine months ended September 30, 2022 consisted of option exercise proceeds, net of issuance costs. Net cash provided by financing activities for the nine months ended September 30, 2021 consisted primarily of $219.9 million in net proceeds from the sale of 1.4 million common shares issued in connection with our 2021 ATM, which was net of $3.1 million of equity issuance costs and $2.2 million of stamp taxes, as well as option exercise proceeds, net of issuance costs.

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 September 30, 2022, we had cash, cash equivalents and marketable securities of $1,973.1 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.

Inflation

Inflation generally affects us by increasing our cost of labor, clinical trial and manufacturing costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the three and nine months ended September 30, 2022 and 2021.

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 September 30, 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 September 30, 2022, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

During the quarter ended September 30, 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-K, 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: November 1, 2022

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

Dated: November 1, 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: November 1, 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: November 1, 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 September 30, 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)

November 1, 2022

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

November 1, 2022