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To the General Meeting of
CRISPR Therapeutics AG, Zug

Basle, February 21, 2023

Report of the statutory auditor

Report on the audit of the consolidated financial statements

Opinion

We have audited the accompanying consolidated financial statements of CRISPR Therapeutics AG and its subsidiaries (the Group), which comprise the consolidated balance sheets as of December 31, 2022 and 2021, and the related consolidated statements of operations and comprehensive (loss) income, of shareholders' equity, and of cash flows for each of the three years in the period ended December 31, 2022, and the related notes, including a summary of significant accounting policies.

In our opinion, the accompanying consolidated financial statements present fairly, in all material respects, the financial position of the Group as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles (US GAAP) and comply with Swiss law.

Basis for opinion

We conducted our audit in accordance with Swiss law, Swiss Standards on Auditing (SA-CH) and the standards of the Public Company Accounting Oversight Board (United States) (PCAOB standards). Our responsibility is to express an opinion on these consolidated financial statements based on our audit and our responsibilities under those provisions and standards are further described in the "Auditor's responsibilities for the audit of the consolidated financial statements" section of our report. We are a public accounting firm and are independent of the Group in accordance with the provisions of Swiss law U.S. federal securities law, together with the requirements of the Swiss audit profession, the U.S. Securities and Exchange Commission and the PCAOB and we have fulfilled our other ethical responsibilities in accordance with these requirements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a reasonable basis for our opinion.

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Critical audit matter

The critical audit matter communicated below is the matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the Audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which it relates.

Estimation of Variable Consideration for ongoing Collaboration Agreements

Description of the Matter	As discussed in Note 8 to the consolidated financial statements, the Company has multiple ongoing collaboration agreements which include rights to future payments totaling up to approximately $2.2 billion as of December 31, 2022 that are payable upon the achievement of various developmental, regulatory and commercial milestones related to certain programs under development. These future payments represent variable consideration that is included in the transaction price for these collaboration agreements to the extent that the Company determines it is probable that a significant revenue reversal of cumulative revenue recognized under the contract will not occur. When the Company cannot conclude that it is probable that a significant revenue reversal of cumulative revenue under the contract will not occur, the Company constrains the related variable consideration resulting in its exclusion from the transaction price. The Company's estimation of variable consideration to be constrained impacts the reported amounts of revenue and deferred revenue within the consolidated financial statements. In determining the portion of the transaction price to be constrained, management considers the probability and uncertainty of whether the related developmental, regulatory and commercial milestones will be achieved given the nature of clinical development and the stage of the underlying programs. This assessment is performed at each reporting period. In making this evaluation, management considers both internal and external information available including information from industry publications, the stage of development of the underlying programs and other relevant factors. Changes to the constraint of variable consideration can have a material effect on the amount of revenue recognized in the financial reporting period. As a result, auditing the accounting for the application of constraint to variable consideration required complex auditor judgement.
How We Addressed the Matter in Our Audit	We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's revenue recognition process. For example, we tested controls over management's estimation of the total transaction price for its collaboration agreements including those related to the application of constraint to variable consideration associated with future developmental, regulatory and commercial milestones.

To audit the Company's judgements related to the application of constraint to variable consideration, we performed audit procedures that included, among others, evaluating the Company's judgements related to the probability of achieving the related future developmental, regulatory and commercial milestones. To evaluate the Company's estimated probability of achieving developmental, regulatory and commercial milestones, we considered the nature of clinical development and the stage of development of the underlying programs in relation to relevant external data and compared the probabilities of achieving the milestones to current industry trends and available information from other guideline companies within the same industry and other relevant factors. We also discussed the probability of achieving the milestones in relation to each program's phase of development with the Company's research and development managers.

Other information

The Board of Directors is responsible for the other information. The other information comprises the information included in the annual report, but does not include the consolidated financial statements, the stand-alone financial statements, the remuneration report and our auditor's reports thereon.

Our opinion on the consolidated financial statements does not cover the other information and we do not express any form of assurance conclusion thereon.

In connection with our audit of the consolidated financial statements, our responsibility is to read the other information and, in doing so, consider whether the other information is materially inconsistent with the consolidated financial statements or our knowledge obtained in the audit or otherwise appears to be materially misstated.

If, based on the work we have performed, we conclude that there is a material misstatement of this other information, we are required to report that fact. We have nothing to report in this regard.

Board of Directors' responsibilities for the consolidated financial statements

The Board of Directors is responsible for the preparation and fair presentation of the consolidated financial statements in accordance with US GAAP and the provisions of Swiss law, and for such internal control as the Board of Directors determines is necessary to enable the preparation of consolidated financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the consolidated financial statements, the Board of Directors is responsible for assessing the Group's ability to continue as a going concern, disclosing, as applicable, matters related to going concern, and using the going concern basis of accounting unless the Board of Directors either intends to liquidate the Group or to cease operations, or has no realistic alternative but to do so.

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Auditor's responsibilities for the audit of the consolidated financial statements
Our objectives are to obtain reasonable assurance about whether the consolidated financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with Swiss law, SA-CH and PCAOB standards will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these consolidated financial statements.

As part of an audit in accordance with Swiss law, SA-CH and PCAOB standards, we exercise professional judgment and maintain professional skepticism throughout the audit. We also:

- Identify and assess the risks of material misstatement of the consolidated financial statements, whether due to fraud or error, design and perform audit procedures responsive to those risks, and obtain audit evidence that is sufficient and appropriate to provide a basis for our opinion. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.
- Obtain an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances.
- Evaluate the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made.
- Conclude on the appropriateness of the Board of Directors' use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on the Group's ability to continue as a going concern. If we conclude that a material uncertainty exists, we are required to draw attention in our auditor's report to the related disclosures in the consolidated financial statements or, if such disclosures are inadequate, to modify our opinion. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report. However, future events or conditions may cause the Group to cease to continue as a going concern.
- Evaluate the overall presentation, structure and content of the consolidated financial statements, including the disclosures, and whether the consolidated financial statements represent the underlying transactions and events in a manner that achieves fair presentation.
- Obtain sufficient appropriate audit evidence regarding the financial information of the entities or business activities within the Group to express an opinion on the consolidated financial statements. We are responsible for the direction, supervision and performance of the group audit. We remain solely responsible for our audit opinion.

We communicate with the Board of Directors and the Audit Committee regarding, among other matters, the planned scope and timing of the audit and significant audit findings, including any significant deficiencies in internal control that we identify during our audit.

We also provide the Board of Directors and the Audit Committee with a statement that we have complied with relevant ethical requirements regarding independence, and to communicate with them all relationships and other matters that may reasonably be thought to bear on our independence, and where applicable, actions taken to eliminate threats or safeguards applied.

From the matters arising from the audit of the consolidated financial statements that were communicated or required to be communicated to the Board of Directors and the Audit Committee, we determine those matters that related to accounts or disclosures that are material to the consolidated financial statements and involved especially challenging, subjective, or complex auditor judgment in the current period and are therefore critical audit matters.

Report on other legal and regulatory requirements

In accordance with Art. 728a para. 1 item 3 CO and PS-CH 890, we confirm that an internal control system exists, which has been designed for the preparation of the consolidated financial statements according to the instructions of the Board of Directors.

We recommend that the consolidated financial statements submitted to you be approved.

We have served as the Group's auditor since 2013.

Ernst & Young Ltd

Simon Zogg (Qualified Signature)

Licensed audit expert
(Auditor in charge)

Faidra Ekati Lygerou (Qualified Signature)

Certified Auditor Accountant (Greece)

Enclosures

- Financial statements (consolidated balance sheets as of December 31, 2022 and 2021, and the related consolidated statements of operations and comprehensive (loss) income, of shareholders' equity, and of cash flows for each of the three years in the period ended December 31, 2022)

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

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 211,885	$ 923,031
Marketable securities	1,603,433	1,456,098
Accounts receivable	—	305
Prepaid expenses and other current assets	37,708	38,079
Total current assets	1,853,026	2,417,513
Property and equipment, net	163,634	137,575
Marketable securities, non-current	53,130	—
Intangible assets, net	71	125
Restricted cash	11,635	16,913
Operating lease assets	156,921	174,460
Other non-current assets	4,640	5,291
Total assets	$ 2,243,057	$ 2,751,877
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 27,428	$ 14,816
Accrued expenses	77,682	91,003
Deferred revenue, current	—	1,011
Accrued tax liabilities	135	724
Operating lease liabilities	15,842	12,158
Other current liabilities	20	171
Total current liabilities	121,107	119,883
Deferred revenue, non-current	12,323	12,323
Operating lease liabilities, net of current portion	228,179	212,872
Other non-current liabilities	5,969	7,339
Total liabilities	367,578	352,417
Commitments and contingencies (Note 9)		
Shareholders' equity:		
Common shares, CHF 0.03 par value, 150,347,467 and 145,364,335 shares authorized at December 31, 2022 and 2021, respectively, 78,692,766 and 77,170,382 shares issued at December 31, 2022 and 2021, respectively, 78,512,450 and 76,990,066 shares outstanding at December 31, 2022 and 2021, respectively.	2,441	2,391
Treasury shares, at cost, 180,316 shares at December 31, 2022 and 2021, respectively	(63)	(63)
Additional paid-in capital	2,734,838	2,598,114
Accumulated deficit	(846,090)	(195,915)
Accumulated other comprehensive loss	(15,647)	(5,067)
Total shareholders' equity	1,875,479	2,399,460
Total liabilities and shareholders' equity	$ 2,243,057	$ 2,751,877

See accompanying notes to these consolidated financial statements.

CRISPR Therapeutics AG
Consolidated Statements of Operations and Comprehensive (Loss) Income
(In thousands, except share and per share data)

	Years Ended December 31,		
	2022	2021	2020
Revenue:			
Collaboration revenue	$ 436	$ 913,081	$ 543
Grant revenue	762	1,882	176
Total revenue	1,198	914,963	719
Operating expenses:			
Research and development	461,645	340,567	221,382
General and administrative	102,464	99,690	85,747
Collaboration expense, net	110,250	101,178	48,025
Total operating expenses	674,359	541,435	355,154
(Loss) income from operations	(673,161)	373,528	(354,435)
Other income:			
Other income, net	22,661	6,003	6,379
Total other income, net	22,661	6,003	6,379
Net (loss) income before income taxes	(650,500)	379,531	(348,056)
Benefit (provision) for income taxes	325	(1,870)	(809)
Net (loss) income	(650,175)	377,661	(348,865)
Foreign currency translation adjustment	(80)	(11)	40
Unrealized loss on marketable securities	(10,500)	(4,973)	(130)
Comprehensive (loss) income	$ (660,755)	$ 372,677	$ (348,955)
Net (loss) income per common share — basic	$ (8.36)	$ 4.97	$ (5.29)
Basic weighted-average common shares outstanding	77,746,575	75,948,686	65,949,672
Net (loss) income per common share — diluted	$ (8.36)	$ 4.70	$ (5.29)
Diluted weighted-average common shares outstanding	77,746,575	80,393,496	65,949,672

See accompanying notes to these consolidated financial statements.

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

	Common Shares		Treasury Shares		Additional			
	Shares	CHF 0.03 Par Value	Shares	Amount, at cost	Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive (Loss) Income	Total Shareholders' Equity
Balance at December 31, 2019	60,783,799	$ 1,847	250,226	$ (63)	$ 1,162,345	$ (224,711)	$ 7	$ 939,425
Issuance of common shares, net of issuance costs of $46.4 million	11,412,519	366	—	—	973,015	—	—	973,381
Vesting of restricted shares	204,650	7	—	—	—	—	—	7
Exercise of vested options, net of issuance costs of $1.2 million	1,482,636	57	(37,080)	—	32,718	—	—	32,775
Purchase of common stock under ESPP	13,410	—	—	—	694	—	—	694
Stock-based compensation expense	—	—	—	—	66,018	—	—	66,018
Issuance of common stock for license agreements	17,830	—	(17,830)	—	889	—	—	889
Other comprehensive loss	—	—	—	—	—	—	(90)	(90)
Net loss	—	—	—	—	—	(348,865)	—	(348,865)
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	455,440	15	—	—	—	—	—	15
Exercise of vested options, net of issuance costs of $2.6 million	1,245,071	54	(15,000)	—	35,820	—	—	35,874
Purchase of common stock under ESPP	21,590	—	—	—	2,095	—	—	2,095
Stock-based compensation expense	—	—	—	—	102,390	—	—	102,390
Other comprehensive loss	—	—	—	—	—	—	(4,984)	(4,984)
Net income	—	—	—	—	—	377,661	—	377,661
Balance at December 31, 2021	76,990,066	$ 2,391	180,316	$ (63)	$ 2,598,114	$ (195,915)	$ (5,067)	$ 2,399,460
Issuance of common shares	12,365	—	—	—	970	—	—	970
Vesting of restricted shares	237,932	8	—	—	—	—	—	8
Exercise of vested options, net of issuance costs of $0.9 million	1,235,528	42	—	—	35,771	—	—	35,813
Purchase of common stock under ESPP	36,559	—	—	—	2,036	—	—	2,036
Stock-based compensation expense	—	—	—	—	97,947	—	—	97,947
Other comprehensive loss	—	—	—	—	—	—	(10,580)	(10,580)
Net loss	—	—	—	—	—	(650,175)	—	(650,175)
Balance at December 31, 2022	78,512,450	$ 2,441	180,316	$ (63)	$ 2,734,838	$ (846,090)	$ (15,647)	$ 1,875,479

See accompanying notes to these consolidated financial statements.

CRISPR Therapeutics AG
Consolidated Statements of Cash Flows
(In thousands)

	Years Ended December 31,		
	2022	**2021**	**2020**
Operating activities			
Net (loss) income	$ (650,175)	$ 377,661	$ (348,865)
Reconciliation of net (loss) income to net cash used in operating activities:			
Depreciation and amortization	24,172	17,953	9,184
Equity-based compensation	97,947	102,390	66,018
Other non-cash items, net	12,470	14,109	1,857
Changes in:			
Accounts receivable	305	(161)	(45)
Prepaid expenses and other assets	1,598	(13,912)	17,338
Accounts payable and accrued expenses	5,164	37,514	25,747
Deferred revenue	(1,011)	(783)	1,381
Operating lease assets and liabilities	15,310	9,506	(473)
Other liabilities, net	(1,521)	(5,305)	(10,508)
Net cash (used in) provided by operating activities	(495,741)	538,972	(238,366)
Investing activities			
Purchase of property, plant and equipment	(37,188)	(81,705)	(18,358)
Purchases of marketable securities	(1,417,800)	(1,509,327)	(593,998)
Maturities of marketable securities	1,196,333	555,602	71,186
Net cash used in investing activities	(258,655)	(1,035,430)	(541,170)
Financing activities			
Proceeds from issuance of common shares, net of issuance costs	970	213,267	982,289
Proceeds from exercise of options and ESPP contributions, net of issuance costs	37,622	37,678	33,863
Net cash provided by financing activities	38,592	250,945	1,016,152
Effect of exchange rate changes on cash	(80)	(11)	40
(Decrease) increase in cash	(715,884)	(245,524)	236,656
Cash, cash equivalents and restricted cash, beginning of period	939,944	1,185,468	948,812
Cash, cash equivalents and restricted cash, end of period	$ 224,060	$ 939,944	$ 1,185,468
Supplemental disclosure of non-cash investing and financing activities			
Property and equipment purchases in accounts payable and accrued expenses	$ 2,121	$ 8,348	$ 3,412
Equity issuance costs in accounts payable and accrued expenses	$ 99	$ 334	$ 9,590

Reconciliation to amounts within the consolidated balance sheets	As of December 31,		
	2022	**2021**	**2020**
Cash and cash equivalents	211,885	923,031	1,168,620
Prepaid expenses and other current assets	540	—	—
Restricted cash	11,635	16,913	16,848
Total	$ 224,060	$ 939,944	$ 1,185,468

See accompanying notes to these consolidated financial statements.

CRISPR Therapeutics AG
Notes to Consolidated Financial Statements

1. Organization and Operations

CRISPR Therapeutics AG ("CRISPR" or the "Company") was incorporated on October 31, 2013 in Basel, Switzerland. The Company was established to translate CRISPR/Cas9, a genome editing technology, into transformative gene-based medicines for the treatment of serious human diseases. The foundational intellectual property underlying the Company's operations was licensed to the Company in April 2014. The Company devotes substantially all of its efforts to product research and development activities, initial market development and raising capital. The Company's principal offices are in Zug, Switzerland, with the U.S. headquarters for research and development in Boston, Massachusetts, additional research and development based in San Francisco, CA, and a cell therapy manufacturing facility in Framingham, Massachusetts.

The Company is subject to risks common to companies in the biotechnology industry, including but not limited to, risks of failure of preclinical studies and clinical trials, the need to obtain marketing approval for any drug product candidate that it may identify and develop, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations and ability to transition from pilot-scale manufacturing to large-scale production of products.

The Company had an accumulated deficit of $846.1 million as of December 31, 2022 and has financed its operations to date from a series of preferred shares and convertible loan issuances, proceeds obtained from its initial public offering, subsequent public offerings of its common shares, as well as upfront fees and milestones received under its collaboration and joint venture arrangements. The Company will require additional capital to fund its research and development and ongoing operating expenses.

As of December 31, 2022, the Company had cash, cash equivalents and marketable securities of $1,868.4 million. While the Company was in a net income position in certain previous years due to upfronts associated with the Company's collaborations with Vertex Pharmaceuticals Incorporated and certain of its subsidiaries, or Vertex, the Company has a history of recurring losses and expects to continue to incur losses for the foreseeable future. The Company expects its cash and cash equivalents will be sufficient to fund current planned operations for at least the next twenty-four months.

The full extent of the impact of the coronavirus pandemic on the Company's business, operations and financial results will depend on numerous evolving factors that we may not be able to accurately predict. See Item 1A: "Risk Factors" section set forth in this Annual Report on Form 10-K for additional details. At this stage, the impact on the Company's results has not been significant.

2. Summary of Significant Accounting Policies and Basis of Presentation

Basis of Presentation and Use of Estimates

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America, or GAAP, and include the accounts of the Company and its wholly-owned subsidiaries as of December 31, 2022. All intercompany accounts and transactions have been eliminated. Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification, or ASC, and Accounting Standards Updates, or ASUs, of the Financial Accounting Standards Board.

Beginning in 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 consolidated statements of operations and comprehensive (loss) income. As a result, collaboration costs under the Vertex Agreements accounted for under ASC 808 for years ended December 31, 2021 and 2020 have been reclassified to conform to the current presentation. No subtotals in the prior period's consolidated financial statements were impacted. Refer to Note 8 to these consolidated financial statements for further discussion on the Vertex Agreements.

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, revenue recognition, equity-based compensation expense and reported amounts of research and development 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.

Segment Information

The Company and the Company's chief operating decision maker, namely, the chief executive officer, view the Company's operations and manage its business as one operating segment, which is the business of discovering, developing and commercializing therapies derived from or incorporating genome-editing technology.

Foreign Currency Translation and Transactions

The majority of the Company's operations occur in entities that have the U.S. dollar as their functional currency. Non-U.S. dollar denominated functional currency subsidiaries have assets and liabilities translated into U.S. dollars at rates of exchange in effect at the end of the year. Revenue and expense amounts are translated using the average exchange rates for the period. Net unrealized gains and losses resulting from foreign currency translation are included in "Accumulated other comprehensive (loss) income." Net foreign currency exchange transaction gains or losses are included in "Other income, net" on the Company's consolidated statement of operations, the impact of which is not significant.

Cash and Cash Equivalents

The Company considers all highly liquid investments with maturities of three months or less from the purchase date to be cash equivalents. As of December 31, 2022 and 2021, the Company had $211.9 million and $923.0 million in cash and cash equivalents, respectively.

Restricted Cash

As of December 31, 2022 and 2021, the Company had $12.2 million and $16.9 million, respectively, in restricted cash representing letters of credit securing the Company's obligations under certain leased facilities, as well as certain credit card arrangements. The letters of credit are secured by cash held in a restricted depository account, with $0.5 million and $0.0 million, respectively, included in prepaid expenses and other current assets in the accompanying consolidated balance sheets as of December 31, 2022 and 2021, and $11.6 million and $16.9 million, respectively, included in restricted cash in the accompanying consolidated balance sheets as of December 31, 2022 and 2021.

Marketable Securities

As of December 31, 2022 and 2021, the Company had $1,656.6 million and $1,456.1 million, respectively in marketable securities. The Company's investment strategy is focused on capital preservation. The Company invests in instruments that meet the credit quality standards outlined in the Company's investment policy. The Company classifies marketable securities with a remaining maturity, when purchased, of greater than three months as available-for-sale. Marketable securities are classified as current assets on the consolidated balance sheets if the marketable securities are available to be converted into cash to fund current operations.

Marketable securities in an unrealized loss position for greater than one year with a remaining maturity date greater than one year are classified as non-current assets.

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. Debt securities are carried at fair value with the unrealized gains and losses included in other comprehensive (loss) income as a component of stockholders' equity until realized. Any premium arising at purchase is amortized to interest expense over the period of the earliest call date, and any discount arising at purchase is accreted to interest income over the life of the instrument. Realized gains and losses on debt securities are determined using the specific identification method and are included in other income, net.

The Company assesses its available-for-sale debt securities under the available-for-sale debt security impairment model in ASU 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Statements*, or ASC 326, as of each reporting date in order to determine if a portion of any decline in fair value below carrying value recognized on its available-for-sale debt securities is the result of a credit loss. The Company records credit losses in the consolidated statements of operations and comprehensive loss as credit loss expense within other expense, net, which is limited to the difference between the fair value and the amortized cost of the security. To date, the Company has not recorded any credit losses on its available-for-sale debt securities.

Other Receivables

Amounts due from collaboration partners where an arrangement is accounted for under ASC 808 are considered other receivables and are included within prepaid and other current assets in the consolidated balance sheets. Other receivables consisted of $11.2 million and $8.4 million as of December 31, 2022 and 2021, respectively and are due from Vertex. Other receivables are recorded at invoiced amounts due under the Vertex collaboration agreement, as described further in Note 8. Vertex is a creditworthy entity that maintains an ongoing relationship with the Company and as such, the Company does not have an allowance for estimated credit losses recorded related to these other receivables.

Concentrations of Credit Risk and Off-balance Sheet Risk

Financial instruments that potentially subject the Company to concentrations of credit risk are primarily cash, cash equivalents and marketable securities. The Company's cash is held in accounts with financial institutions that management believes are creditworthy. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. The Company has no financial instruments with off-balance sheet risk of loss.

Fair Value of Financial Instruments

The Company has certain financial assets and liabilities recorded at fair value which have been classified as Level 1, 2 or 3 within the fair value hierarchy as described in the accounting standards for fair value measurements:

Level 1 — Quoted prices in active markets that are accessible at the market date for identical unrestricted assets or liabilities.

Level 2 — Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs for which all significant inputs are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Items measured at fair value on a recurring basis include marketable securities (see Note 3, *Marketable Securities*, and Note 4, *Fair Value Measurement*). The carrying amount of accounts receivable, other receivables, accounts payable and accrued expenses as reported on the consolidated balance sheets as of December 31, 2022 and 2021, approximate fair value, due to the short-term duration of these instruments.

Property and Equipment

Property and equipment are recorded at cost, less accumulated depreciation. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred. Upon disposal, the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss is included in the results of operations. Depreciation is recorded using the straight-line method over the estimated useful lives of the respective assets, which are as follows:

Asset	Estimated useful life
Computer equipment	3 years
Furniture, fixtures and other	5 years
Laboratory equipment	5 years
Leasehold improvements	Shorter of useful life or remaining lease term

Impairment of Long-lived Assets

The Company reviews long-lived assets when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparison of the book values of the assets to future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book value of the assets exceed their fair value, which is measured based on the projected discounted future net cash flows arising from the assets.

Revenue Recognition

The Company records revenue in accordance with ASC Topic 606, *Revenue from Contracts with Customers*, or ASC 606. ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases and collaboration arrangements. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps:

1) Identify the contract with the customer

A contract with a customer exists when (i) the Company enters into an enforceable contract with a customer that defines each party's rights regarding the goods or services to be transferred and identifies the related payment terms, (ii) the contract has commercial substance and (iii) the Company determines that collection of substantially all consideration for goods and services that are transferred is probable based on the customer's intent and ability to pay the promised consideration.

2) Identify the performance obligations in the contract

Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct, whereby the customer can benefit from the good or service either on its own or together with other available resources, and are distinct in the context of the contract, whereby the transfer of the good or service is separately identifiable from other promises in the contract. To the extent a contract includes multiple promised goods and services, the Company must apply judgment to determine whether promised goods and services are capable of being distinct and distinct in the context of the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation.

3) Determine the transaction price

The transaction price is determined based on the consideration to which the Company will be entitled in exchange for transferring goods and services to the customer. To the extent the transaction price includes variable consideration such as research, development, regulatory and commercial milestones, the Company determines if it is probable that it will receive such amounts and there is no risk of a significant revenue reversal. When the Company cannot conclude that receipt of such amounts is probable, the Company constrains the related variable consideration resulting in its exclusion from transaction consideration. In determining the portion of the transaction consideration to be constrained, the Company considers the probability and uncertainty that the related research, developmental, regulatory and commercial milestones will be achieved given the nature of research and clinical development and the stage of the underlying programs. This assessment is performed at each reporting period. In making this evaluation, the Company considers both internal and external information available, including information from industry publications and other relevant factors. Changes to the constraint of variable consideration can have a material effect on the amount of revenue recognized in the period.

4) Allocate the transaction consideration to performance obligations in the contract

If the contract contains a single performance obligation, the entire transaction consideration is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction consideration to each performance obligation on a relative standalone selling price basis unless the transaction consideration is variable and meets

the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation. The consideration to be received is allocated among the separate performance obligations based on relative standalone selling prices. In determining these estimated standalone selling prices, the Company makes a number of significant judgements including, for licenses, management's assumptions regarding probability weighted projected discounted cash flows for each of the collaboration development programs. The estimated standalone selling prices are sensitive to changes in assumptions, such as probabilities of scientific success, discount rate and certain assumptions that form the basis of forecasted cash flows. In developing these assumptions, management considers both internal and external information available, including information from other guideline companies within the same industry and other relevant factors. Changes to these assumptions can have a material effect on the allocation of the transaction consideration to performance obligations, as well as the amount and timing of revenue recognized.

5) Recognize revenue when or as the Company satisfies a performance obligation

The Company satisfies performance obligations over time or at a point in time, depending on the nature of the performance obligation. Revenue is recognized over time if the customer simultaneously receives and consumes the benefits provided by the entity's performance, the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date. If the entity does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer.

Contract Balances

The Company recognizes a contract asset when the Company transfers goods or services to a customer before the customer pays consideration or before payment is due, excluding any amounts presented as an account or other receivable. A contract asset is an entity's right to consideration in exchange for goods or services that the entity has transferred to a customer. The contract liabilities, or deferred revenue, primarily relate to contracts where we have received payment, but we have not yet satisfied the related performance obligations. Contract assets are not significant as of December 31, 2022 and 2021. Contract liabilities recorded as deferred revenue as of December 31, 2022 are $12.3 million, which was unchanged from December 31, 2021. The contract liability recorded as deferred revenue is related to the collaboration agreement with Vertex described in Note 8.

Collaboration Arrangements

The Company records the elements of its collaboration agreements that represent joint operating activities in accordance with ASC 808. Accordingly, the elements of the collaboration agreements that represent activities in which both parties are active participants and to which both parties are exposed to the significant risks and rewards that are dependent on the commercial success of the activities, are recorded as collaborative arrangements.

The Company evaluates the proper presentation of the commercial activities and the profit and loss sharing associated with the collaboration agreements. ASC 808 states that when payments between parties in a collaborative arrangement are not within the scope of other authoritative accounting literature, the income statement classification should be based on the nature of the arrangement, the nature of its business operations and the contractual terms of the arrangement. To the extent that these payments are not within the scope of other authoritative accounting literature, the income statement classification for the payments shall be based on an analogy to authoritative accounting literature or if there is no appropriate analogy, a reasonable, rational and consistently applied accounting policy election.

Collaboration costs under the Vertex Agreements accounted for under ASC 808 are presented within "collaboration expense, net" in the consolidated statements of operations and comprehensive (loss) income. Refer to Note 8 to these consolidated financial statements for further discussion on the Vertex Agreements.

Research and Development Expenses

Research and development costs are charged to expense as costs are incurred in performing research and development activities, including salaries and benefits, facilities costs, overhead costs, clinical study and related clinical manufacturing costs, license and milestone fees, contract services and other related costs. Research and development costs, including up-front fees and milestones paid to collaborators, are also expensed as incurred. In circumstances where amounts have been paid in excess of costs incurred, the Company records a prepaid expense. The Company accrues costs for clinical trial activities based upon estimates of the services received and related expenses incurred that have yet to be invoiced by the contract research organizations, clinical study sites, laboratories, consultants or other clinical trial vendors that perform the activities. The Company recognizes the reimbursement associated with collaborative activities to its collaborative partners, excluding collaboration costs under the Vertex Agreements accounted for under ASC 808, as a reduction to research and development expense in the period the services are provided. Costs associated with collaborative activities to collaborative partners accounted for under ASC 808 and included in research and development expense was not significant for the years ended December 31, 2022, 2021 and 2020

Leases

The Company accounts for its leases in accordance with ASC 842, *Leases*, or ASC 842. At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company does not have financing leases.

Operating lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. Prospectively, the Company will adjust the right-of-use assets for straight-line rent expense or any incentives received and remeasure the lease liability at the net present value using the same incremental borrowing rate that was in effect as of the lease commencement or transition date.

The Company has elected not to recognize leases with an original term of one year or less on the balance sheet. The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to renew a lease are not included in the Company's assessment unless there is reasonable certainty of renewal.

Assumptions made by the Company at the commencement date are re-evaluated upon occurrence of certain events, including a lease modification. A lease modification results in a separate contract when the modification grants the lessee an additional right of use not included in the original lease and when lease payments increase commensurate with the standalone price for the additional right of use. When a lease modification results in a separate contract, it is accounted for in the same manner as a new lease.

Equity Based Compensation Expense

The Company's share-based compensation programs grant awards that have included stock options, restricted stock units and restricted stock awards. Grants are awarded to employees and non-employees, including directors.

The Company accounts for its stock-based compensation awards in accordance with ASC Topic 718, *Compensation—Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees and non-employee directors, including grants of employee stock options and restricted stock units and modifications to existing stock options, to be recognized in the consolidated statements of operations and comprehensive (loss) income based on their fair values. The Company uses the Black-Scholes option pricing model to determine the fair value of options granted.

The Company accounts for forfeitures as they occur instead of estimating forfeitures at the time of grant and revising those estimates in subsequent periods if actual forfeitures differ from its estimates. Stock-based compensation expense recognized in the financial statements is based on awards for which performance or service conditions are expected to be satisfied.

The Company's stock-based awards are subject to service or performance-based vesting conditions. Compensation expense related to awards to employees, directors and non-employees with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term. Compensation expense related to awards to employees with performance-based vesting conditions is recognized based on the grant date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable.

The Company expenses restricted stock unit awards to employees based on the fair value of the award on a straight-line basis over the associated service period of the award.

The Company estimates the fair value of its option awards to employees, directors and non-employees using the Black-Scholes option pricing model, which requires the input of subjective assumptions, including (i) the expected stock price volatility, (ii) the calculation of expected term of the award, (iii) the risk-free interest rate and (iv) expected dividends. Due to the lack of complete company-specific historical and implied volatility data for the full expected term of the stock-based awards, the Company bases its estimate of expected volatility on a representative group of publicly traded companies in addition to its own volatility data. For these analyses, the Company selected companies with comparable characteristics to its own, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The Company computes historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available. The Company has estimated the expected term of its employee stock options using the "simplified" method, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option, due to its lack of sufficient historical data. The risk-free interest rates for periods within the expected term of the option are based on the U.S. Treasury securities with a maturity date

commensurate with the expected term of the associated award. The Company has never paid, and does not expect to pay, dividends in the foreseeable future.

Patent Costs

Costs to secure and prosecute patent applications and other legal costs related to the protection of the Company's intellectual property are expensed as incurred and are classified as general and administrative expenses in the Company's consolidated statements of operations.

Income Taxes

Income taxes are recorded in accordance with ASC Topic 740, *Income Taxes*, or ASC 740, which provides for deferred taxes using an asset and liability approach. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial reporting and tax reporting basis of assets and liabilities and are measured using enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company has evaluated available evidence and concluded that the Company may not realize all the benefit of its deferred tax assets; therefore, a valuation allowance has been established for the amount of the deferred tax assets that the Company does not believe is more likely than not to be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2022 and 2021, the Company does not have any significant uncertain tax positions. The Company's practice is to recognize interest and/or penalties related to income tax matters in income tax expense. See Note 14 for further details.

Comprehensive (Loss) Income

Comprehensive (loss) income consists of net income or loss and other comprehensive (loss) income. Other comprehensive (loss) income consists of foreign currency translation adjustments and unrealized losses on marketable securities.

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 equivalent shares outstanding for the period, including any dilutive effect from outstanding stock options and restricted stock units using the treasury stock method. See Note 12 for further details.

New Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the 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.

3. Marketable Securities

A summary of the Company's cash equivalents and marketable securities as of December 31, 2022 and 2021, which are recorded at fair value (and excludes $159.3 million and $405.6 million of cash at December 31, 2022 and 2021, respectively) is shown below (in thousands):

December 31, 2022	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash equivalents:				
Money market funds	$ 17,766	$ —	$ —	$ 17,766
Corporate debt securities	2,151	—	(2)	2,149
Certificates of deposit	—	—	—	—
Commercial paper	32,675	—	—	32,675
Total cash equivalents	52,592	—	(2)	52,590
Marketable securities:				
U.S. Treasury securities	—	—	—	—
Corporate debt securities	1,236,770	615	(15,006)	1,222,379
Certificates of deposit	92,417	—	—	92,417
Government-sponsored enterprise securities	79,746	11	(712)	79,045
Commercial paper	263,231	—	(509)	262,722
Total marketable securities	1,672,164	626	(16,227)	1,656,563
Total cash equivalents and marketable securities	$ 1,724,756	$ 626	$ (16,229)	$ 1,709,153

December 31, 2021	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash equivalents:				
Money market funds	$ 507,386	$ —	$ —	$ 507,386
Corporate debt securities	—			—
Certificates of deposit	—	—	—	—
Commercial paper	9,997	—	(1)	9,996
Total cash equivalents	517,383	—	(1)	517,382
Marketable securities:				
U.S. Treasury securities	16,238	6	(52)	16,192
Corporate debt securities	1,173,659	10	(4,903)	1,168,766
Certificates of deposit	45,164	—	—	45,164
Government-sponsored enterprise securities	13,334	—	(77)	13,257
Commercial paper	212,805	—	(86)	212,719
Total marketable securities	1,461,200	16	(5,118)	1,456,098
Total cash equivalents and marketable securities	$ 1,978,583	$ 16	$ (5,119)	$ 1,973,480

As of December 31, 2022 and 2021, the aggregate fair value of marketable securities that were in an unrealized loss position for less than twelve months was $628.4 million and $1,311.6 million, respectively. As of December 31, 2022 and 2021, the aggregate fair value of marketable securities that were in an unrealized loss position for more than twelve months was $619.2 million and $4.6 million, respectively. Of this amount, securities totaling $53.1 million as of December 31, 2022 will mature beyond one year. No securities in an unrealized loss position for more than twelve months as of December 31, 2021 will mature beyond one year. The Company has recorded a net unrealized loss of $10.5 million and $5.0 million, respectively, during the years ended December 31, 2022 and 2021 related to its marketable securities, which is included in comprehensive (loss) income on the consolidated statements of operations and comprehensive (loss) income.

The Company determined that there was no material credit risk of the above investments as of December 31, 2022 and 2021. 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 years ended December 31, 2022 and 2021. No available-for-sale debt securities held as of December 31, 2022 had remaining maturities greater than thirty months.

4. Fair Value Measurement

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 December 31, 2022 and 2021 (in thousands):

	Fair Value Measurements at December 31, 2022			
	Total	Level 1	Level 2	Level 3
Cash and cash equivalents:				
Cash	$ 159,295	$ 159,295	$ —	$ —
Money market funds	17,766	17,766	—	—
Corporate debt securities	2,149	—	2,149	—
Certificates of deposit	—	—	—	—
Commercial paper	32,675	—	32,675	—
Marketable securities:				
U.S. Treasury securities	—	—	—	—
Corporate debt securities	1,222,379	—	1,222,379	—
Certificates of deposit	92,417	—	92,417	—
Government-sponsored enterprise securities	79,045	—	79,045	—
Commercial paper	262,722	—	262,722	—
Other non-current assets	2,212	—	—	2,212
Total	$ 1,870,660	$ 177,061	$ 1,691,387	$ 2,212

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

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

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

5. Property and Equipment, net

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

	As of December 31,	
	2022	2021
Computer equipment	$ 3,618	$ 1,757
Furniture, fixtures, and other	8,109	4,371
Laboratory equipment	37,897	30,123
Leasehold improvements	141,680	86,735
Construction work in process	6,162	52,396
Total property and equipment, gross	197,466	175,382
Accumulated Depreciation	(33,832)	(37,807)
Total property and equipment, net	$ 163,634	$ 137,575

Depreciation expense for the year ended December 31, 2022, 2021 and 2020 was $24.1 million, $17.9 million, and $9.1 million, respectively.

6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	As of December 31,	
	2022	2021
Payroll and employee-related costs	$ 19,241	$ 23,661
Research costs	46,187	47,986
Licensing fees	983	138
Professional fees	4,927	4,720
Intellectual property costs	3,936	6,120
Accrued property and equipment	1,244	7,113
Other	1,164	1,265
Total	$ 77,682	$ 91,003

7. Leases

In June 2015, the Company entered into a lease agreement for the lease of research facility space in Cambridge, Massachusetts, with a commencement date of November 15, 2015. The lease was subsequently amended in both 2017 and 2020 and expired in 2022.

In May 2016, the Company entered into a sublease agreement for its primary office and research facility in Cambridge, Massachusetts, with a commencement date of December 23, 2016. The sublease was subsequently amended in 2021 and expired in 2022.

In May 2019, the Company entered into a lease agreement for office facility space in Cambridge, Massachusetts, with a commencement date of June 1, 2019, or the 2019 Lease. The lease expires in November 2026, and the Company has an option to extend the term of the lease for an additional five-year period based on certain conditions within the Company's control. The 2019 Lease contains escalating rent clauses which require higher rent payments in future years. The right-of-use asset and corresponding lease liability does not include the additional five-year period under the renewal option as the Company is not reasonably certain to exercise that option.

In December 2019, Casebia Therapeutics, Limited Liability Partnership, or Casebia, became a wholly-owned subsidiary of the Company. In connection therewith, Casebia assigned its sublease for an office and research facility in Cambridge, Massachusetts to the Company. The sublease was subsequently amended in 2021 and expired in 2022.

In May 2020, the Company entered into a lease agreement for a cell therapy manufacturing facility in Framingham, Massachusetts, or the Framingham Lease, for clinical and commercial production of the Company's investigational cell therapy product candidates. The Framingham Lease expires in March 2036 and the Company has an option to extend the term of the lease for two additional seven-year periods. The right-of-use asset and corresponding lease liability does not include the additional seven-year periods under the renewal option as the Company is not reasonably certain to exercise that option.

In July 2020, the Company entered into a lease agreement for an office and laboratory facility in Boston, Massachusetts, with a commencement date of June 1, 2021, or the 2020 Lease. At lease commencement, the Company recorded a right-of-use asset of $149.8 million and a corresponding operating lease liability of $147.9 million. Tenant incentives of $49.2 million were recorded as a reduction to the operating lease asset and liability at lease commencement. The lease expires in March 2034 and the Company has an option to extend the term of the lease for two additional five-year periods. The right-of-use asset and corresponding lease liability does not include the additional five-year periods under the renewal option as the Company is not reasonably certain to exercise that option.

The Company also rents certain office space in Zug, Switzerland, on a short-term basis for which a right-of-use asset and liability are not recorded, in accordance with the practical expedient elected.

The Company has embedded leases in certain research and license agreements for which the Company has recorded a right of use asset and liability. These arrangements are not significant in comparison to the Company's total operating lease assets and liabilities. In addition, the Company has identified certain short-term leases embedded within its manufacturing contracts which are not recorded on the Company's balance sheet in accordance with the practical expedient elected.

The Company identified and assessed the following estimates in recognizing the right-of-use asset and corresponding liability:

- *Expected lease term*: The expected lease term includes noncancelable lease periods and, when applicable, periods covered by an option to extend the lease if the Company is reasonably certain to exercise that option, as well as periods covered by an option to terminate the lease if the Company is reasonably certain not to exercise that option.
- *Incremental borrowing rate*: As the discount rates in the Company's leases are not implicit, the Company estimated the incremental borrowing rate based on the rate of interest the Company would have to pay to borrow a similar amount on a collateralized basis over a similar term.

The following table summarizes the lease assets and liabilities as of December 31, 2022 and 2021 (in thousands):

	As of December 31,	
	2022	2021
Assets		
Operating lease assets	$ 156,921	$ 174,460
Total lease assets	156,921	174,460
Liabilities		
Current		
Operating lease liabilities	15,842	12,158
Non-current		
Operating lease liabilities, net of current portion	228,179	212,872
Total lease liabilities	$ 244,021	$ 225,030

The following table summarizes operating lease costs included in research and development and general and administrative expense, as well as sublease income for the twelve months ended December 31, 2022, 2021 and 2020 (in thousands):

	Years Ended December 31,		
	2022	2021	2020
Operating lease costs	$ 34,896	$ 22,520	$ 14,342
Short-term lease costs	824	11,087	7,339
Variable lease costs	11,882	8,402	6,368
Sublease income	—	(5,253)	(587)
Net lease cost	$ 47,602	$ 36,756	$ 27,462

The following table summarizes the maturity of undiscounted payments due under lease liabilities and the present value of those liabilities as of December 31, 2022 (in thousands):

	Total
2023	29,270
2024	26,526
2025	26,251
2026	26,745
2027	25,927
Thereafter	205,495
Total	$ 340,214
Present value adjustment	(96,193)
Present value of lease liabilities	$ 244,021

The following table summarizes the lease term (in years) and discount rate for operating leases as of December 31, 2022 and 2021:

	As of December 31,	
	2022	2021
Weighted-average remaining lease term	11.8	12.4
Weighted-average discount rate	5.9%	5.9%

The following table summarizes the cash paid for amounts included in the measurement of lease liabilities for the years ended December 31, 2022, 2021 and 2020 (in thousands):

	Years Ended December 31,		
	2022	2021	2020
Cash paid for amounts included in measurement of lease liabilities:			
Operating cash flows used in operating leases	$ (17,004)	$ (19,753)	$ (13,161)
Operating lease non-cash items:			
Right-of-use assets (decreased) increased through lease modifications and reassessments	1,208	(14,230)	3,169
Right-of-use assets obtained in exchange for operating lease liabilities	—	152,486	13,956
Leasehold improvements paid directly by landlord	19,252	30,500	—

8. 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 December 31, 2022, the Company is eligible to receive remaining potential future milestones of $775.0 million under the 2019 Collaboration Agreement.

In April 2021, the Company and Vertex agreed to amend and restate the JDA and entered into an Amended and Restated Joint Development and Commercialization Agreement, or the "A&R Vertex JDCA," pursuant to which the parties agreed to, among other things, (a) adjust the governance structure for the collaboration and adjust the responsibilities of each party thereunder, whereby Vertex shall lead and have all decision making (i.e., control) in relation to the exa-cel program prospectively; (b) adjust the allocation of net profits and net losses between the parties with respect to exa-cel (formerly known as CTX001) only, which will be allocated 40% to the Company and 60% to Vertex, prospectively; and (c) exclusively license (subject to the Company's reserved rights to conduct certain activities) certain intellectual property rights to Vertex relating to the specified product candidates and products (including 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, collaborative arrangements as defined under ASC 808 and research and development costs as defined under ASC 730, *Research and Development*, or ASC 730.

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 twelve months ended December 31, 2022 and 2020. For the twelve months ended December 31, 2021, the Company recognized $12.0 million in revenue related to a milestone under the 2019 Agreements.

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

Revenue recognized in connection with the Vertex Agreements

Revenue recognized under the Vertex Agreements for the year ended December 31, 2022 was not material. Revenue recognized under the Vertex Agreements for the year ended December 31, 2021 was $913.1 million and was comprised of (i) revenue related to the exclusive worldwide license for exa-cel of $900.0 million, (ii) revenue related to the second DM1 milestone under the 2019 Agreements of $12.0 million, and (iii) revenue recognized in connection with research and development services. Revenue recognized under the Vertex Agreements for the year ended December 31, 2020 was not material.

As of December 31, 2022 and 2021 there was no current deferred revenue related to the collaboration with Vertex, respectively. As of December 31, 2022 and 2021, there was $12.3 million of non-current deferred revenue, respectively, related to the collaboration with Vertex. 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 December 31, 2022. There is uncertainty that the events to obtain the research and developmental milestones will be achieved given the nature of clinical development and the stage of the CRISPR/Cas9 technology. The remaining research, development and regulatory milestones will be constrained until it is probable that a significant revenue reversal will not occur. Commercial milestones and royalties relate predominantly to a license of intellectual property and are determined by sales or usage-based thresholds. The commercial milestones and royalties are accounted for under the royalty recognition constraint and will be accounted for as constrained variable consideration. The Company applies the royalty recognition constraint for each commercial milestone and will not recognize revenue for each until the subsequent sale of a licensed product (achievement of each) occurs.

Accounting Analysis under ASC 808

In connection with the Vertex Agreements, the Company identified the following collaborative elements, which are accounted for under ASC 808: (i) development and commercialization services for shared products, including any transition services related to 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 consolidated statements of operations and comprehensive (loss) income.

During the years ended December 31, 2022, 2021 and 2020, the Company recognized $110.3 million, $101.2 million, and $48.0 million of collaboration expense, net, related to the Vertex Agreements, respectively. Research and development expense for the years ended December 31, 2022, 2021 and 2020 is net of $37.8 million, $47.4 million, and $27.6 million of reimbursements from Vertex, respectively.

Under the A&R Vertex JDCA, the Company has an option to defer its portion of specified costs on the exa-cel program in excess of $110.3 million for the year ended December 31, 2022. Vertex may only recover any such deferred amounts as an offset against future profitability of the exa-cel program, determined on an annual basis in accordance with the A&R Vertex JDCA. Any such deferred amounts are capped at a specified maximum amount per year. For the year ended December 31, 2022, the Company exercised its option to defer $36.1 million of its share of costs incurred under the A&R Vertex JDCA. These deferred costs will be recognized by the Company when recoverability of such deferred amounts by Vertex is probable and the amount can be reasonably estimated. As of December 31, 2022, no such deferred amounts have been recognized.

9. Commitments and Contingencies

Intellectual Property Agreements

Charpentier License Agreements

In April 2014, the Company entered into certain technology license agreements with Dr. Emmanuelle Charpentier pursuant to which the Company licensed certain intellectual property rights under joint ownership from Dr. Charpentier to develop and commercialize products for the treatment or prevention of human diseases. In connection therewith, Dr. Charpentier is entitled to receive nominal clinical milestone payments, low single digit percentage of sublicensing payments received under any sublicense agreement with a third party, and low single-digit percentage royalties based on annual net sales of licensed products and services by the Company and its affiliates and sublicensees.

Patent Assignment Agreement

In November 2014, the Company entered into a patent assignment agreement with Dr. Charpentier, Dr. Ines Fonfara, and Vienna (collectively, the "Assignors"), pursuant to which the Company was assigned all rights, title and interest in and to certain patent rights claimed in the U.S. Patent Application No.61/905,835. As a result, the Assignors are entitled to receive certain low single digit clinical milestone payments and low single digit royalties based on annual net sales of licensed products and licensed services by the Company, its affiliates and sublicensees.

During the years ended December 31, 2022, 2021 and 2020, the Company paid an immaterial amount of fees to Dr. Charpentier under the Charpentier License Agreements and the Assignors under the Patent Assignment Agreement, which were recorded as research and development expense.

Research, Manufacturing and License 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 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. Vertex also has the option to conduct research at their own cost in certain defined areas that, if beneficial to the exa-cel 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.

Under the A&R Vertex JDCA, the Company deferred $36.1 million of its share of costs incurred under the arrangement for the year ended December 31, 2022, as spending on the exa-cel program exceeded a specified amount. 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. These deferred costs on the exa-cel program will be accrued for when it is probable that a liability has been incurred and the amount can be reasonably estimated. As of December 31, 2022, no contingent payments have been accrued. Refer to Note 8 for further discussion on the Company's arrangements with Vertex.

Other Matters

On December 15, 2016, the Company entered into a Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement (the "Invention Management Agreement") with UC, Vienna, Dr. Charpentier, Intellia Therapeutics, Inc., Caribou Biosciences, Inc., ERS Genomics Ltd. and one of the Company's subsidiaries. Under the Invention Management Agreement, the Company is obligated to share costs related to patent maintenance, defense and prosecution. For the years ended December 31, 2022, 2021 and 2020, the Company incurred $2.2 million, $5.8 million, and $4.5 million, respectively, in shared costs. The Company recorded accrued legal costs from the cost sharing of $1.4 million and 4.0 million as of December 31, 2022 and 2021, respectively. The Company is unable to predict the outcome of these matters and is unable to make a meaningful estimate of the amount or range of loss, if any, that could result from an unfavorable outcome.

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.

10. Share Capital

The Company had 150,347,467 and 145,364,335 authorized common shares as of December 31, 2022 and 2021, respectively, with a par value of CHF 0.03 per share. Share Capital consisted of the following:

		As of December 31,	
Type of Share Capital	**Conditional Capital**	**2022**	**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

Included in registered share capital are 5,025,897 shares registered, of which 4,845,581 shares are held by the Company and its subsidiaries and are reserved for future issuance for financings and 180,316 shares held by the Company and its subsidiaries as treasury shares.

Common Share Issuances

Recent Public Offerings

In July 2020, the Company sold 7.4 million common shares through an underwritten public offering (inclusive of shares sold pursuant to the exercise of the underwriters' option to purchase additional shares) at a public offering price of $70.00 per share for aggregate net proceeds of $484.8 million, which were net of equity issuance costs and stamp tax of $32.5 million.

At-the-Market Offerings

In August 2019, the Company entered into an Open Market Sale Agreement℠ 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 August 2019, 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 $200.0 million, or the 2019 ATM. During the year ended December 31, 2020, the Company issued and sold an aggregate of 2.2 million common shares under the 2019 ATM at an average price of $89.47 per share for aggregate proceeds of $195.5 million, which were net of equity issuance costs of $4.5 million.

In December 2020, 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 $350.0 million, or the 2020 ATM. During the year ended December 31, 2020, the Company issued and sold an aggregate of 1.8 million common shares under the 2020 ATM at an average price of $169.57 per share for aggregate proceeds of $298.0 million, which were net of equity issuance costs of $4.5 million. Additional equity issuance costs for stamp taxes related to shares sold in 2020 related to the 2019 ATM and 2020 ATM were $4.9 million, of which $4.0 million was accrued as of December 31, 2020 and paid in 2021.

In January 2021, the Company issued and sold under the 2020 ATM an aggregate of 0.3 million common shares at an average price of $162.46 per share with aggregate proceeds of $46.7 million, which were net of equity issuance costs of $0.7 million. An additional $0.5 million of stamp taxes related to this amount was paid in 2021.

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 December 31, 2021, the Company issued and sold an aggregate of 1.1 million common shares under the 2021 ATM at an average price of $169.82 per share for aggregate proceeds of $177.8 million, which were net of equity issuance costs of $2.4 million. An additional $1.8 million of stamp taxes related to this amount was paid in 2021.

As of December 31, 2022, the Company has issued and sold an aggregate of 1.1 million common shares under the 2021 ATM at an average price of $168.79 per share for aggregate proceeds of $178.8 million, which were net of equity issuance costs of $2.4 million.

The Common Shares have the following characteristics:

Voting Rights

The holders of common shares are entitled to one vote for each common share held at all meetings of shareholders.

Dividends

The holders of common shares are entitled to receive dividends, if and when resolved upon by the general meeting of shareholders based on a respective proposal by the Board of Directors and provided that the Company disposes of sufficient freely distributable reserves. As of December 31, 2022, no dividends have been declared or paid since the Company's inception.

Liquidation

The holders of the common shares are entitled to share ratably in the Company's assets available for distribution to shareholders in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or upon the occurrence of a deemed liquidation event.

11. Equity-based Compensation

Option and Grant Plans

In April 2015, the Company's shareholders approved the 2015 Stock Option and Grant Plan, or the 2015 Plan, and in July 2016, the Company's shareholders approved the 2016 Stock Option and Incentive Plan, or the 2016 Plan. In May 2018, the Company's shareholders approved the 2018 Stock Option and Incentive Plan, or the 2018 Plan (collectively, the "Plans"). Subsequent to the IPO, no further options were granted under the 2015 Plan. The Plans provide for the issuance of equity awards in the form of restricted shares, options to purchase common shares which may constitute incentive stock options, or ISOs, or non-statutory stock options, or NSOs, unrestricted stock unit grants, and qualified performance and market-based awards to eligible employees, officers, directors, non-employee consultants and other key personnel. Terms of the equity awards, including vesting requirements, are determined by the Company's board of directors, subject to the provisions of the Plans. Options granted by the Company typically vest over four years and have a contractual life of ten years. Restricted stock unit grants typically vest over two to four years. At December 31, 2022, the Company had 26,705,365 common shares authorized for issuance under the 2018 Plan and 10,338,717 common shares available for future grant under the 2018 Plan.

Equity-Based Compensation Expense

The Company recognized stock-based compensation expense totaling $97.9 million, $102.4 million, and $66.0 million during the years ended December 31, 2022, 2021 and 2020, respectively. Stock-based compensation expense by classification within the consolidated statements of operations and comprehensive (loss) income is as follows (in thousands):

	Years Ended December 31,		
	2022	2021	2020
Research and development	$ 53,956	$ 59,683	$ 35,120
General and administrative	43,991	42,707	30,898
Total	$ 97,947	$ 102,390	$ 66,018

As of December 31, 2022, there was $107.9 million and $67.8 million of unrecognized compensation expense related to unvested stock options and restricted stock units, respectively, that is expected to be recognized over a weighted-average period of 2.4 and 2.3 years, respectively.

Stock Options

The fair value of each option issued to employees was estimated at the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Years Ended December 31,		
	2022	2021	2020
Options granted	1,492,589	1,616,255	2,182,773
Weighted-average exercise price	$ 60.19	$ 124.32	$ 68.91
Weighted-average grant date fair value	$ 38.54	$ 77.38	$ 42.28
Assumptions:			
Expected volatility	70.2%	70.3%	69.2%
Expected term (in years)	6.0	6.0	6.0
Risk-free interest rate	2.6%	1.0%	0.6%
Expected dividend yield	0.0%	0.0%	0.0%

The following table summarizes stock option activity under the Company's equity award plans (intrinsic value in thousands):

	Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value
Outstanding at December 31, 2021	7,812,982	$ 58.07	7.4	$ 219,103
Granted	1,492,589	60.19		
Exercised	(1,235,528)	29.66		
Cancelled or forfeited	(839,810)	85.13		
Outstanding at December 31, 2022	7,230,233	$ 60.22	7.0	$ 32,131
Exercisable at December 31, 2022	4,769,450	$ 51.76	6.2	$ 30,915
Vested and expected to vest at December 31, 2022	7,230,233	$ 60.22	7.0	$ 32,131

The total intrinsic value (the amount by which the fair market value exceeded the exercise price) of stock options exercised during the year ended December 31, 2022, 2021 and 2020 was $40.8 million, $119.5 million, and $104.2 million, respectively.

As of December 31, 2022, options to purchase 1,048,911 common shares subject to performance-based vesting conditions were vested, as performance conditions were satisfied in prior years, and there were 170,652 options to purchase common shares subject to performance-based vesting conditions outstanding. Activity related to stock options subject to performance-based vesting conditions is included in the table above.

As of December 31, 2022, options to purchase 150,000 common shares subject to market-based vesting conditions were vested, as market conditions were satisfied in prior years. 150,000 options to purchase common shares subject to market-based vesting conditions were outstanding as of December 31, 2022. Activity related to stock options subject to market-based vesting conditions is included in the table above.

The Company did not grant stock options subject to performance-based or market-based vesting conditions during 2022, 2021, and 2020.

Restricted Stock Units

The following table summarizes the restricted stock unit activity under the Company's equity award plans:

	Shares	Weighted-Average Grant Date Fair Value
Unvested balance at December 31, 2021	934,175	$ 100.14
Granted	853,326	62.31
Vested	(237,932)	83.88
Cancelled or forfeited	(224,384)	91.69
Unvested balance at December 31, 2022	1,325,185	$ 80.13

During the years ended December 31, 2022, 2021 and 2020, the total fair value of restricted stock units vested was $14.3 million, $45.3 million, and $21.6 million, respectively.

During 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. Expense for these awards is being recognized over the requisite service period. As of December 31, 2022, 150,000 of the performance stock units were unvested. Activity related to stock units subject to market-based vesting conditions is included in the table above.

The Company did not grant stock units subject to performance-based or market-based vesting conditions during 2021 and 2020.

Award modifications

Equity award modifications for certain equity awards held by departing employees for the years ended December 31, 2022, 2021 and 2020 were not material to the Company's stock-based compensation expense.

Employee Stock Purchase Plan

On July 19, 2016, the Company's board of directors adopted its 2016 Employee Stock Purchase Plan, or the ESPP Plan, which was subsequently approved by its shareholders and became effective on October 19, 2016. The ESPP Plan authorizes the initial issuance of up to a total of 0.4 million shares of the Company's common stock to participating employees. The Company activated its ESPP Plan on January 1, 2020. The Company issued 36,559 and 21,590 shares under the ESPP Plan during the years ended December 31, 2022 and 2021, respectively.

12. 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 ended (in thousands, except share and per share amounts):

	Year ended December 31,		
	2022	2021	2020
Net (loss) income	$ (650,175)	$ 377,661	$ (348,865)
Basic weighted-average common shares outstanding	77,746,575	75,948,686	65,949,672
Effect of potentially dilutive securities:			
Outstanding options	—	3,990,579	—
Unvested restricted common shares	—	454,231	—
Diluted weighted-average common shares outstanding	77,746,575	80,393,496	65,949,672
Net (loss) income per common share — basic	$ (8.36)	$ 4.97	$ (5.29)
Net (loss) income per common share — diluted	$ (8.36)	$ 4.70	$ (5.29)

The Company did not include the securities in the following table in the computation of the net (loss) income per share calculations because the effect would have been anti-dilutive during each period:

	Year ended December 31,		
	2022	2021	2020
Outstanding options	7,230,233	1,765,881	8,101,980
Unvested restricted common shares	1,325,185	225,904	894,092
ESPP	19,105	6,671	11,257
Total	8,574,523	1,998,456	9,007,329

13. 401(k) Savings Plan

The Company established a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan") in November 2016. The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pretax basis. The Company contributed $3.2 million, $3.4 million, and $1.9 million to the 401(k) Plan for the years ended December 31, 2022, 2021 and 2020, respectively.

14. Income Taxes

The Company is subject to U.S. federal and various state corporate income taxes as well as taxes in foreign jurisdictions for the foreign parent and where foreign subsidiaries have been established.

Net (loss) income before taxes

For the years ended December 31, 2022, 2021 and 2020, the (loss) income before provision for income taxes consist of the following (in thousands):

	Years Ended December 31,		
	2022	2021	2020
Domestic	$ 1,321	$ 4,569	$ 7,630
Foreign	(651,821)	374,962	(355,686)
Total	$ (650,500)	$ 379,531	$ (348,056)

The benefit from (provision for) income taxes consist of the following (in thousands):

	Years Ended December 31,		
	2022	2021	2020
Current income taxes:			
Federal	$ (444)	$ (80)	$ (248)
State	(241)	(42)	(151)
Foreign	—	—	(1)
Total current income taxes	(685)	(122)	(400)
Deferred income taxes:			
Federal	1,010	(1,748)	(409)
State	—	—	—
Foreign	—	—	—
Total deferred income taxes	1,010	(1,748)	(409)
Total income tax benefit (provision)	$ 325	$ (1,870)	$ (809)

A reconciliation of income tax expense computed at the statutory corporate income tax rate to the effective income tax rate for the years ended December 31, 2022, 2021 and 2020 is as follows:

	Years Ended December 31,		
	2022	2021	2020
Income tax expense at statutory rate	11.9%	11.9%	11.9%
State income tax, net of federal benefit	1.2%	(1.0)%	1.0%
Nondeductible expenses	(0.2)%	0.7%	0.1%
Foreign rate differential	(0.1)%	0.6%	(0.1%)
Statutory to US GAAP permanent differences	0.0%	0.0%	0.0%
Stock-based compensation	(0.2)%	(2.5%)	2.3%
Impact of deferred rate change	(0.1)%	0.0%	0.0%
Research credits	3.3%	(4.2)%	3.3%
Change in valuation allowance	(15.8)%	(5.0)%	(18.7%)
Effective income tax rate	—	0.5%	(0.2%)

The federal statutory rate reflects the Switzerland mixed company service rate.

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. The significant components of the Company's deferred tax assets are comprised of the following (in thousands):

	Years Ended December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 118,432	$ 47,190
Accruals and reserves	4,782	5,878
Operating lease liabilities	66,436	61,476
Other deferred tax assets	10,154	6,362
Stock-based compensation	18,034	14,042
Research credit	63,416	37,878
Total deferred tax assets	281,254	172,826
Less valuation allowance	(198,279)	(98,649)
Net deferred tax assets	82,975	74,177
Deferred tax liabilities:		
Depreciation	(41,206)	(28,579)
Operating lease assets	(42,678)	(47,521)
Intangible assets	(18)	(31)
Other deferred tax liabilities	(209)	(192)
Total deferred tax liabilities	(84,111)	(76,323)
Long term deferred taxes	$ (1,136)	$ (2,146)

The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on the Company's history of worldwide operating losses, the Company has concluded that it is more-likely-than-not that the benefit of its U.S. and non-U.S. deferred tax assets will not be realized. Accordingly, as of December 31, 2022 and 2021, the Company has provided a full valuation allowance against its net deferred tax assets in Switzerland and the United Kingdom. The Company has also provided a valuation allowance against the U.S. deferred tax assets that cannot be realized by existing deferred tax liabilities based upon when they are scheduled to reverse. The valuation allowance increased by $99.6 million during 2022, which is primarily attributable to increase in net operating loss carryforwards as a result of current year net loss.

As of December 31, 2022, the Company had no available U.S. federal net operating loss carryforwards. As of December 31, 2022, the Company had available non-U.S. net operating loss carryforwards of $1,979.7 million of which $988.4 million relate to Switzerland, $988.4 million relate to the Canton of Zug, and $2.9 million relate to the Company's wholly-owned subsidiary in the United Kingdom. The net operating losses generated in Switzerland and the Canton of Zug begin to expire in 2027 and the net operating losses generated in the United Kingdom can be carried forward indefinitely.

As of December 31, 2022, the Company had U.S. domestic federal research and development credit carryforwards of $27.3 million that begin to expire in 2039 for federal purposes, which are net of uncertain tax positions of $13.9 million. As of December 31, 2022, the Company had U.S. domestic federal orphan drug credit carryforwards of $22.7 million which begin to expire in 2040 for federal purposes, which are net of uncertain tax positions of $9.8 million. As of December 31, 2022, the Company had U.S. domestic state research and development credit carryforwards of $16.9 million which begin to expire in 2035, which are net of uncertain tax positions of $10.9 million.

ASC 740 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statement by prescribing the minimum recognition threshold and measurement of a tax position taken or expected to be taken in a tax return.

As of December 31, 2022, the Company had gross unrecognized tax benefits of $34.5 million of which $32.3 million would favorably impact the effective tax rate if recognized. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2022, 2021 and 2020, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's consolidated statements of operations and comprehensive loss.

The aggregate changes in gross unrecognized tax benefits were as follows (in thousands):

	Years Ended December 31,		
	2022	2021	2020
Balance at beginning of year	$ 21,395	$ 11,967	$ 5,231
Increases for tax positions taken during current period	10,439	9,911	7,004
Increases for tax positions taken in prior periods	2,702	—	—
Decreases for tax positions taken during current period	—	—	—
Decreases for tax positions taken in prior periods	—	(483)	(268)
Balance at end of year	$ 34,536	$ 21,395	$ 11,967

The Company files income tax returns in the U.S. federal jurisdiction, Massachusetts, California and certain non-U.S. jurisdictions. The Company is subject to U.S. federal, Massachusetts, California and non-U.S. income tax examinations by authorities for tax years ending after December 31, 2018. Research credits generated in prior tax years that are closed for examination may still be adjusted upon future examination if they have or will be used in a future period. The Company is subject to income tax examinations by authorities in its non-U.S. jurisdictions for all years.