Report of the statutory auditor

with consolidated financial statements as of 31 December 2021 of

CRISPR Therapeutics AG, Zug

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To the General Meeting of
CRISPR Therapeutics AG, Zug

Basle, 15 February 2022

Report of the statutory auditor on the consolidated financial statements

Opinion

As statutory auditor, we have audited the consolidated financial statements of CRISPR Therapeutics AG and its subsidiaries (pages F-4 to F-35), which comprise the consolidated balance sheets as of 31 December 2021 and 31 December 2020, and the related consolidated statements of operations and comprehensive (loss) income, consolidated statements of shareholders' equity, consolidated statements of cash flows, and notes to the consolidated financial statements for each of the three years in the period ended 31 December 2021.

In our opinion, the consolidated financial statements present fairly, in all material respects, the consolidated financial position of the Group as of 31 December 2021 and 31 December 2020, and the consolidated results of its operations and its cash flows for each of the three years in the period ended 31 December 2021, in accordance with U.S. generally accepted accounting principles and comply with Swiss law.

Board of Directors' responsibility

The Board of Directors is responsible for the preparation of the consolidated financial statements in accordance with U.S. generally accepted accounting principles and the requirements of Swiss law. This responsibility includes designing, implementing and maintaining an internal control system relevant to the preparation of consolidated financial statements that are free from material misstatement, whether due to fraud or error. The Board of Directors is further responsible for selecting and applying appropriate accounting policies and making accounting estimates that are reasonable in the circumstances.

Auditor's responsibility

Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm and are required to be independent with respect to the Company. We conducted our audits in accordance with Swiss law, Swiss Auditing Standards and the standards of the Public Company Accounting Oversight Board (United States) (PCAOB). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free from material misstatement, whether due to fraud or error.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the consolidated financial statements. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatement of the consolidated financial statements, whether due to fraud or error. In making those risk assessments, the auditor considers the internal control system relevant to the entity's preparation of the consolidated financial statements in order to design audit procedures that are appropriate in the circumstances.

An audit also includes evaluating the appropriateness of the accounting policies used and the reasonableness of accounting estimates made, as well as evaluating the overall presentation of the consolidated financial statements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the consolidated financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate 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 critical audit matters 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 matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Estimation of Variable Consideration for ongoing Collaboration Agreements

Description of the Matter

As discussed in Note 9 to the consolidated financial statements, the Company has multiple ongoing collaboration agreements which include rights to future payments totaling up to $2.2 billion as of 31 December 2021 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.

Revenue Recognition for Collaboration and Joint Development Agreement with Vertex Pharmaceuticals Incorporated

Description of the Matter

As discussed in Note 9 to the consolidated financial statements, on 16 April 2021 the Company entered into an amendment to its joint development agreement with Vertex Pharmaceuticals Inc., referred to as the "A&R Vertex JDCA", which resulted in a payment of $900 million and the recognition of $900 million of revenue by the Company for the year ended 31 December 2021.

Accounting for the A&R Vertex JDCA required the Company to make certain significant judgements, including the determination of the standalone selling price of an identified performance obligation. The estimated standalone selling price for an identified performance obligation reflect management's assumptions regarding probability weighted projected discounted cash flows for an underlying collaboration development program. The estimated standalone selling price was sensitive to changes in certain assumptions within the discounted cash flow model such as the discount rate, and certain assumptions that form the basis of the forecasted cash flows (e.g., price per patient). In developing these assumptions, management considered 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 estimated standalone selling price of the performance obligation, impacting the amount and timing of revenue recognized. As a result,

	auditing the estimate of the standalone selling price for an identified performance obligation required especially 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 process to determine the significant assumptions described above with respect to the estimation of the standalone selling price of a performance obligation. To audit the Company's revenue recognition related to the A&R Vertex JDCA, we performed audit procedures that included, among others, evaluating management's estimate of the standalone selling price of an identified performance obligation. For example, we evaluated the probability weighted projected discounted cash flow assumptions used by the Company in developing the estimated standalone selling price by comparing the significant assumptions described above to current industry trends using available information from other guideline companies within the same industry and other relevant factors. We also performed a sensitivity analysis of the significant assumptions to evaluate the impact that the change in the estimated standalone selling price of an identified performance obligation resulting from changes in the significant assumptions would have on the amount and timing of revenue recognized during the period. We involved our valuation professionals to assist in the assessment of the estimation methodology and the significant valuation assumptions used in determining the estimated standalone selling price of an identified performance obligation.

Report on other legal and regulatory requirements

We are a public accounting firm registered with the Swiss Federal Audit Oversight Authority (FAOA) and the PCAOB and we confirm that we meet the legal requirements on licensing according to the Auditor Oversight Act (AOA). We are independent with respect to the Group in accordance with Swiss law (article 728 CO and article 11 AOA) and U.S. federal securities laws as well as the applicable rules and regulations 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.

In accordance with article 728a para. 1 item 3 CO and Swiss Auditing Standard 890, we confirm that an internal control system exists, which has been designed for the preparation of 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)

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

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 923,031	$ 1,168,620
Marketable securities	1,456,098	521,713
Accounts receivable	305	144
Prepaid expenses and other current assets	38,079	26,143
Total current assets	2,417,513	1,716,620
Property and equipment, net	137,575	42,160
Intangible assets, net	125	180
Restricted cash	16,913	16,848
Operating lease assets	174,460	50,865
Other non-current assets	5,291	1,293
Total assets	$ 2,751,877	$ 1,827,966
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 14,816	$ 9,094
Accrued expenses	91,003	53,782
Deferred revenue, current	1,011	2,341
Accrued tax liabilities	724	10,473
Operating lease liabilities	12,158	11,362
Other current liabilities	171	7,207
Total current liabilities	119,883	94,259
Deferred revenue, non-current	12,323	11,776
Operating lease liabilities, net of current portion	212,872	50,067
Other non-current liabilities	7,339	7,630
Total liabilities	352,417	163,732
Commitments and contingencies (Note 8)		
Shareholders' equity:		
Common shares, CHF 0.03 par value, 145,364,335 and 115,172,786 shares authorized at December 31, 2021 and 2020, respectively, 77,170,382 and 74,110,160 shares issued at December 31, 2021 and 2020, respectively, 76,990,066 and 73,914,844 shares outstanding at December 31, 2021 and 2020, respectively.	2,391	2,277
Treasury shares, at cost, 180,316 and 195,316 shares at December 31, 2021 and 2020, respectively	(63)	(63)
Additional paid-in capital	2,598,114	2,235,679
Accumulated deficit	(195,915)	(573,576)
Accumulated other comprehensive loss	(5,067)	(83)
Total shareholders' equity	2,399,460	1,664,234
Total liabilities and shareholders' equity	$ 2,751,877	$ 1,827,966

See accompanying notes to these consolidated financial statements.

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

	Years Ended December 31,		
	2021	2020	2019
Revenue:			
Collaboration revenue (1)	$ 913,081	$ 543	$ 289,590
Grant revenue	1,882	176	—
Total revenue	914,963	719	289,590
Operating expenses:			
Research and development (2)	438,633	266,946	179,362
General and administrative	102,802	88,208	63,488
Total operating expenses	541,435	355,154	242,850
Income (loss) from operations	373,528	(354,435)	46,740
Other income (expense):			
Loss from equity method investment	—	—	(5,467)
Other income, net	6,003	6,379	26,033
Total other income, net	6,003	6,379	20,566
Net income (loss) before income taxes	379,531	(348,056)	67,306
Provision for income taxes	(1,870)	(809)	(448)
Net income (loss)	377,661	(348,865)	66,858
Foreign currency translation adjustment	(11)	40	15
Unrealized loss on marketable securities	(4,973)	(130)	—
Comprehensive income (loss)	$ 372,677	$ (348,955)	$ 66,873
Net income (loss) per common share — basic	$ 4.97	$ (5.29)	$ 1.23
Basic weighted-average common shares outstanding	75,948,686	65,949,672	54,392,304
Net income (loss) per common share — diluted	$ 4.70	$ (5.29)	$ 1.17
Diluted weighted-average common shares outstanding	80,393,496	65,949,672	56,932,798
(1) Including the following amounts of revenue from a related party, see Note 9	$ —	$ —	$ 746
(2) Including the following amounts of research and development from a related party, see Note 9	$ —	$ —	$ 14,459

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 Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Shareholders' Equity
	Shares	CHF 0.03 Par Value	Shares	Amount, at cost				
Balance at December 31, 2018	51,852,862	$ 1,584	307,936	$ (57)	$ 682,245	$ (291,569)	$ (8)	$ 392,195
Issuance of common shares, net of issuance costs of $25.1 million	7,704,068	230	(47,297)	—	414,559	—	—	414,789
Vesting of restricted shares	68,009	2	—	—	41	—	—	43
Exercise of vested options, net of issuance costs of $0.3 million	1,158,860	31	(10,413)	(6)	15,976	—	—	16,001
Stock-based compensation expense	—	—	—	—	49,524	—	—	49,524
Other comprehensive income	—	—	—	—	—	—	15	15
Net income	—	—	—	—	—	66,858	—	66,858
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

See accompanying notes to these consolidated financial statements.

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

	Years Ended December 31,		
	2021	**2020**	**2019**
Operating activities			
Net income (loss)	$ 377,661	$ (348,865)	$ 66,858
Reconciliation of net income (loss) to net cash used in operating activities:			
Depreciation and amortization	17,953	9,184	4,725
Equity-based compensation	102,390	66,018	44,057
Loss from equity method investment in Casebia	—	—	5,467
Gain from consolidation of Casebia	—	—	(16,000)
Net amortization of premiums and discounts on marketable securities	14,109	1,857	—
Changes in:			
Accounts receivable	(161)	(45)	(11)
Prepaid expenses and other assets	(13,912)	17,338	(32,618)
Accounts payable and accrued expenses	37,514	25,747	5,025
Deferred revenue	(783)	1,381	(45,146)
Operating lease assets and liabilities	9,506	(473)	(663)
Other liabilities, net	(5,305)	(10,508)	24,983
Net cash provided by (used in) operating activities	538,972	(238,366)	56,677
Investing activities			
Purchase of property, plant and equipment	(81,705)	(18,358)	(6,684)
Net cash and restricted cash received in connection with the acquisition of Casebia	—	—	8,009
Purchases of marketable securities	(1,509,327)	(593,998)	—
Maturities of marketable securities	555,602	71,186	—
Net cash (used in) provided by investing activities	(1,035,430)	(541,170)	1,325
Financing activities			
Proceeds from issuance of common shares, net of issuance costs	213,267	982,289	415,019
Proceeds from exercise of options and ESPP contributions, net of issuance costs	37,678	33,863	15,964
Net cash provided by financing activities	250,945	1,016,152	430,983
Effect of exchange rate changes on cash	(11)	40	15
(Decrease) increase in cash	(245,524)	236,656	489,000
Cash, cash equivalents and restricted cash, beginning of period	1,185,468	948,812	459,812
Cash, cash equivalents and restricted cash, end of period	$ 939,944	$ 1,185,468	$ 948,812
Supplemental disclosure of non-cash investing and financing activities			
Property and equipment purchases in accounts payable and accrued expenses	$ 8,348	$ 3,412	$ 1,811
Equity issuance costs in accounts payable and accrued expenses	$ 334	$ 9,590	$ 295

Reconciliation to amounts within the consolidated balance sheets	As of December 31,		
	2021	**2020**	**2019**
Cash and cash equivalents	923,031	1,168,620	943,771
Restricted Cash	16,913	16,848	5,041
Total	$ 939,944	$ 1,185,468	$ 948,812

See accompanying notes to these 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 and operations are in Cambridge, 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 $195.9 million as of December 31, 2021 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 substantial additional capital to fund its research and development and ongoing operating expenses.

As of December 31, 2021, the Company had cash, cash equivalents and marketable securities of $2,379.1 million. While the Company was in a net income position in the current and 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, 2021. 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.

Prior to December 13, 2019, the Company accounted for its 50% investment in Casebia Therapeutics, Limited Liability Partnership, or Casebia, under the equity method. As described in Note 9, on December 13, 2019, Casebia became a wholly-owned subsidiary and, as a result, the Company consolidated Casebia's financial results from that date forward.

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 in one operating segment, which is the business of discovering, developing and commercializing therapies derived from or incorporating genome-editing technology.

Foreign Currency Translation and Transactions

The 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 income (loss)." Net foreign currency exchange transaction gains or losses are included in "Other income (expense), 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, 2021 and 2020, the Company had $923.0 million and $1,168.6 million in cash and cash equivalents, respectively.

Restricted Cash

As of December 31, 2021, the Company had $16.9 million in restricted cash representing letters of credit securing the Company's obligations under certain leased facilities, as well as certain credit card arrangements, which was unchanged from December 31, 2020. The letters of credit are secured by cash held in a restricted depository account and recorded in restricted cash in the accompanying consolidated balance sheet as of December 31, 2021.

Marketable Securities

As of December 31, 2021 and 2020, the Company had $1,456.1 million and $521.7 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. As a result, the Company classified all of these securities as current assets even though the stated maturity of some individual securities may be one year or more beyond the balance sheet date.

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 income (loss) 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 (expense), net.

Effective January 1, 2020, the Company adopted ASU 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Statements*, or ASC 326. As the Company did not hold available-for-sale debt securities upon adoption, no related transition provisions were applicable to the Company upon adoption.

The Company assesses its available-for-sale debt securities under the available-for-sale debt security impairment model in 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, *Collaborative Arrangements*, or ASC 808, are considered other receivables and are included within prepaid and other current assets in the consolidated balance sheet. Other receivables consisted of $8.4 million and $10.7 million as of December 31, 2021 and 2020, respectively and are due from Vertex. Other receivables are recorded at invoiced amounts due under the Vertex collaboration agreement, as described further in Note 9. 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, 2021 and 2020, 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, 2021 and 2020. Contract liabilities recorded as deferred revenue as of December 31, 2021 and 2020 are $12.3 million and $12.2 million, respectively. The change in contract assets and contract liabilities recorded as deferred revenue is related to the collaboration agreement with Vertex described in Note 9.

Collaboration Arrangements

The Company records the elements of its collaboration agreements that represent joint operating activities in accordance with ASC 808, *Collaborative arrangements*, or 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.

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 as a reduction to research and development expense in the period the services are provided.

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 income (loss) 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, 2021 and 2020, 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 Income (Loss)

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

Variable Interest Entities

The Company reviews each legal entity formed by parties related to the Company to determine whether or not the Company has a variable interest in the entity and whether or not the entity would meet the definition of a variable interest entity, or VIE, in accordance with ASC Topic 810, *Consolidation*, or ASC 810. If the entity is a VIE, the Company assesses whether or not the Company is the primary beneficiary of that VIE based on a number of factors, including (i) which party has the power to direct the activities that most significantly affect the VIE's economic performance, (ii) the parties' contractual rights and responsibilities pursuant to any contractual agreements and (iii) which party has the obligation to absorb losses or the right to receive benefits from the VIE. If the Company determines it is the primary beneficiary of a VIE, the Company consolidates the financial statements of the VIE into the Company's consolidated financial statements at the time that determination is made. The Company evaluates whether it continues to be the primary beneficiary of any consolidated VIEs on a quarterly basis. If the Company were to determine that it is no longer the primary beneficiary of a consolidated VIE, or no longer has a variable interest in the VIE, it would deconsolidate the VIE in the period that the determination is made.

If the Company determines it is the primary beneficiary of a VIE that meets the definition of a business, the Company measures the assets, liabilities and noncontrolling interests of the newly consolidated entity at fair value in accordance with ASC Topic 805, *Business Combinations*, or ASC 805, at the date the reporting entity first becomes the primary beneficiary.

In February 2016, Casebia, was formed in the United Kingdom. In March 2016, upon consummation of the joint venture ("JV"), Bayer Healthcare LLC and certain of its affiliates ("Bayer") and the Company each received a 50% equity interest in the entity in exchange for their contributions to the entity. The Company determined that Casebia was considered a VIE and concluded that it is not the primary beneficiary of the VIE. As such, the Company has not historically consolidated Casebia's results into the consolidated financial statements.

As described in Note 9, on December 13, 2019, Casebia became a fully-owned subsidiary and, as a result, the Company consolidated Casebia's financial results accordingly from that point forward.

Net Income (Loss) Per Share Attributable to Common Shareholders

Basic net income (loss) per share is calculated by dividing net income (loss) attributable to common shareholders by the weighted-average number of common shares outstanding during the period. Diluted net income (loss) per share is calculated by dividing the net income (loss) 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. Unless otherwise discussed below, 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.

ASU No. 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes, or ASU 2019-12*, which is intended to simplify the accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. The Company adopted ASU 2019-12 on January 1, 2021. The adoption of ASU 2019-12 did not have a material impact on the Company's financial position or results of operations upon adoption.

3. Marketable Securities

A summary of the Company's cash equivalents and marketable securities as of December 31, 2021 and 2020, which are recorded at fair value (and excludes $405.6 million and $395.1 million of cash at December 31, 2021 and 2020, respectively) is shown below (in thousands):

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

December 31, 2020	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash equivalents:				
Money market funds	$ 742,958	$ —	$ —	$ 742,958
Corporate debt securities	2,526	1	(24)	2,503
Certificates of deposit	12,527	—	—	12,527
Commercial paper	15,549	—	—	15,549
Total cash equivalents	773,560	1	(24)	773,537
Marketable securities:				
U.S. Treasury securities	47,976	3	—	47,979
Corporate debt securities	324,569	43	(156)	324,456
Certificates of deposit	25,162	—	—	25,162
Government-sponsored enterprise securities	33,738	5	(2)	33,741
Commercial paper	90,375	—	—	90,375
Total marketable securities	521,820	51	(158)	521,713
Total cash equivalents and marketable securities	$ 1,295,380	$ 52	$ (182)	$ 1,295,250

As of December 31, 2021 and 2020, the aggregate fair value of marketable securities that were in an unrealized loss position for less than twelve months was $1,311.6 million and $280.3 million, respectively. As of December 31, 2021, the aggregate fair value of marketable securities that were in an unrealized loss position for more than twelve months was $4.6 million. As of December 31, 2020, no marketable securities were in an unrealized loss position for more than twelve months. The Company has recorded a net unrealized loss of $5.0 million and $0.1 million, respectively, during the years ended December 31, 2021 and 2020 related to its marketable securities, which is included in comprehensive income (loss) on the consolidated statements of operations and comprehensive income (loss). No net unrealized loss was recorded related to its marketable securities for the year ended December 31, 2019.

The Company determined that there was no material credit risk of the above investments as of December 31, 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, 2021 and 2020.

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, 2021 and 2020 (in thousands):

	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

	Fair Value Measurements at December 31, 2020			
	Total	Level 1	Level 2	Level 3
Cash and cash equivalents:				
Cash	$ 395,083	$ 395,083	$ —	$ —
Money market funds	742,958	742,958	—	—
Corporate debt securities	2,503	—	2,503	—
Certificates of deposit	12,527	—	12,527	—
Commercial paper	15,549	—	15,549	—
Marketable securities:				
U.S. Treasury securities	47,979	—	47,979	—
Corporate debt securities	324,456	—	324,456	—
Certificates of deposit	25,162	—	25,162	—
Government-sponsored enterprise securities	33,741	—	33,741	—
Commercial paper	90,375	—	90,375	—
Other non-current assets	600	—	—	600
Total	$ 1,690,933	$ 1,138,041	$ 552,292	$ 600

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,	
	2021	2020
Computer equipment	$ 1,757	$ 727
Furniture, fixtures, and other	4,371	3,416
Laboratory equipment	30,123	25,353
Leasehold improvements	86,735	25,473
Construction work in process	52,396	8,366
Total property and equipment, gross	175,382	63,335
Accumulated Depreciation	(37,807)	(21,175)
Total property and equipment, net	$ 137,575	$ 42,160

Depreciation expense for the year ended December 31, 2021, 2020 and 2019 was $17.9 million, $9.1 million, and $4.7 million, respectively.

6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	As of December 31,	
	2021	2020
Payroll and employee-related costs	$ 23,661	$ 22,402
Research costs	47,986	21,684
Licensing fees	138	1,401
Professional fees	4,720	1,670
Intellectual property costs	6,120	3,625
Accrued property and equipment	7,113	2,835
Other	1,265	165
Total	$ 91,003	$ 53,782

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, or the 2015 Lease. The lease was subsequently amended in both 2017 and 2020 and now expires in 2022 with no further option to extend. The 2015 Lease contains escalating rent clauses, which require higher rent payments in future years.

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, or the 2016 Sublease. The sublease was subsequently amended in 2021 and now expires in 2022. The right-of-use assets and right-of-use liabilities were adjusted in the second quarter of 2021, accordingly. The 2016 Sublease contains escalating rent clauses, which require higher rent payments in future years.

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 became a wholly-owned subsidiary of the Company. In connection therewith, Casebia assigned its sublease for an office and research facility in Cambridge, Massachusetts, or the 2019 Sublease, to the Company. The sublease was subsequently amended in 2021 and now expires in 2022 with no further option to extend. The right-of-use assets and right-of-use liabilities were adjusted in the second quarter of 2021, accordingly. The 2019 Sublease contains escalating rent clauses which require higher rent payments in future years.

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, or the 2020 Lease. The 2020 Lease commenced in the second quarter of 2021, and 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 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 lease expires in March 2034 and the Company has an option to extend the term of the lease for two additional five-year periods.

In addition, the Company 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 for those leases commencing prior to January 1, 2019 did not change with the adoption of ASC 842. The expected lease term for leases commencing after the adoption of ASC 842 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, 2021 and 2020 (in thousands):

	As of December 31,	
	2021	2020
Assets		
Operating lease assets	$ 174,460	$ 50,865
Total lease assets	174,460	50,865
Liabilities		
Current		
Operating lease liabilities	12,158	11,362
Non-current		
Operating lease liabilities, net of current portion	212,872	50,067
Total lease liabilities	$ 225,030	$ 61,429

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, 2021, 2020 and 2019 (in thousands):

	Years Ended December 31,		
	2021	2020	2019
Operating lease costs	$ 22,520	$ 14,342	$ 8,067
Short-term lease costs	11,087	7,339	4,554
Variable lease costs	8,402	6,368	4,282
Sublease income	(5,253)	(587)	(525)
Net lease cost	$ 36,756	$ 27,462	$ 16,378

The following table summarizes the maturity of undiscounted payments due under lease liabilities and the present value of those liabilities as of December 31, 2021 (in thousands):

	Total
2022	18,256
2023	26,633
2024	26,137
2025	26,347
2026	26,844
Thereafter	227,528
Total	$ 351,745
Present value adjustment	(126,715)
Present value of lease liabilities	$ 225,030

The following table summarizes the lease term (in years) and discount rate for operating leases as of December 31, 2021 and 2020:

	As of December 31,	
	2021	2020
Weighted-average remaining lease term	12.4	9.1
Weighted-average discount rate	5.9%	9.3%

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

	Years Ended December 31,		
	2021	2020	2019
Cash paid for amounts included in measurement of lease liabilities:			
Operating cash flows used in operating leases	$ (19,753)	$ (13,161)	$ (8,420)
Operating lease non-cash items:			
Right-of-use assets (decreased) increased through lease modifications and reassessments	(14,230)	3,169	826
Right-of-use assets obtained in exchange for operating lease liabilities	152,486	13,956	18,088
Leasehold improvements paid directly by landlord	30,500	—	—

8. 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, 2021, 2020 and 2019, 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 defined in Note 9 below. In addition, Vertex has the option to conduct research at their own cost in certain defined areas that, if beneficial to the CTX001 program and ultimately achieves regulatory approval, then the Company could owe Vertex certain milestone payments aggregating to high eight digits, subject to certain limitations on the profitability of the CTX001 program. Refer to Note 9 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, 2021, 2020 and 2019, the Company incurred $5.8 million, $4.5 million and $2.9 million, respectively, in shared costs. The Company recorded accrued legal costs from the cost sharing of $4.0 million and $2.5 million as of December 31, 2021 and 2020, 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.

9. 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 on July 23, 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 this collaboration. 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, 2021, the Company is eligible to receive remaining potential future milestones of $775.0 under the 2019 Collaboration Agreement.

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

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

Accounting for the Vertex Agreements

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

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

Accounting Analysis Under ASC 606

Accounting for the A&R Vertex JDCA

Identification of the Contract

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

Identification of Performance Obligations

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

Determination of Transaction Price

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

Allocation of Transaction Price to Performance Obligations

The selling price of the performance obligation was determined based on the Company's ESSP. The Company developed the ESSP for the CTX001 Exclusive License with the objective of determining the price at which it would sell such an item if it were to be sold regularly on a standalone basis.

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

Recognition of Revenue

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

Accounting for the 2019 Agreements

Identification of the Contract

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.

Identification of Performance Obligations

The Company concluded the following material promises were both capable of being distinct and distinct within the context of the 2019 Agreements and represented separate performance obligations: (i) an exclusive license for worldwide rights for DMD gene editing products, or DMD License; (ii) an exclusive license for worldwide rights for DM1 gene editing products, or DM1 License; (iii) the performance of specified guide RNA research for DM1, or DM1 R&D Services; (iv) a material right representing the option to obtain a co-exclusive development and commercialization license for a specified target, or Specified Target Option; (v) three material rights representing the option for up to three exclusive licenses to develop and commercialize the collaboration targets, or Collaboration Target Options; and (vi) the waiving of Vertex's material right associated with its option to a fourth exclusive license in connection with the Company's reacquisition of exclusive rights to the specified target.

Determination of Transaction Price

The initial overall transaction price was determined based on the remaining transaction price from the 2015 Agreements, as well as the transaction price from the 2019 Agreements. The initial transaction price included variable consideration estimated using the most likely amount methodology. The Company determined the initial transaction price totaling $268.6 million was comprised of: (i) $57.8 million of pre-existing deferred revenue from the 2015 Agreements; (ii) non-cash consideration of $10.0 million related to the waiving of Vertex's material right associated with its option to a fourth exclusive license in connection with the Company's reacquisition of exclusive rights to the specified target; (iii) an upfront payment of $175.0 million; (iv) variable consideration of $25.0 million which represented the Company's estimate related to a near-term research and development milestone for which the Company determined that it is not probable that a significant reversal of cumulative consideration will occur at the onset of the transaction; and (v) variable consideration of $0.8 million which represents the Company's estimate of payments from Vertex for DM1 R&D Services.

In December 2021, the Company achieved a milestone under the 2019 Collaboration Agreement. In connection therewith, the Company adjusted the transaction price to include $12.5 million in previously constrained variable consideration. The milestone was allocated to the performance obligations using the relative standalone selling price method, and revenue of $12.0 million was

recognized for amounts allocated to fully satisfied performance obligations. Amounts allocated to unsatisfied performance obligations of $0.5 million were included in deferred revenue.

The Company determined that all other possible variable consideration resulting from milestones and royalties discussed above was fully constrained as of December 31, 2021. The Company will re-evaluate the transaction price in each reporting period.

Allocation of Transaction Price to Performance Obligations

The selling price of each performance obligation was determined based on the Company's ESSP. The Company developed the ESSP for all the performance obligations included in the Vertex Agreements with the objective of determining the price at which it would sell such an item if it were to be sold regularly on a standalone basis. The Company then allocated the transaction price to each performance obligation on a relative standalone selling price basis.

The ESSP for the DMD License and DM1 License was determined to be $224.6 million and $76.2 million, respectively. The ESSP was determined based on probability and present value adjusted cash flows from projected worldwide net profit for each of the respective programs 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. On a relative basis, $151.1 million and $51.3 million of the initial transaction price was allocated to the DMD License and DM1 License, respectively.

The ESSP for the Specified Target Option material right was determined to be $17.5 million, which was based on the incremental discount between (i) the value of the probability and present value adjusted cash flows from the equal sharing of projected worldwide net profit increased by the value of the option provided to Vertex less (ii) the expected exercise price at the time of option exercise. The present value adjusted cash flows also considered projections based on internal forecasts, industry data, and information from other guideline companies within the same industry and other relevant factors. On a relative basis $11.8 million of the initial transaction price was allocated to the Specified Target Option material right.

The ESSP for each of the three Collaboration Target Option material rights was determined to be $25.0 million, $22.2 million and $22.2 million, respectively, which was determined based on the probability and present value adjusted cash flows from milestone payments owed for exclusive licenses, less the price paid to exercise each option. On a relative basis, $46.7 million of the initial transaction price was allocated to the Collaboration Target Option material rights.

The aforementioned ESSPs reflect the level of risk and expected probability of success inherent in the nature of the associated research area.

The ESSP for the waiving of Vertex's material right associated with its option to a fourth exclusive license under the 2015 Agreements was determined to be $10.0 million, or the contractual value of the option. On a relative basis, $6.7 million of the initial transaction price was allocated to the waiving of Vertex's material right associated with its option to a fourth exclusive license under the 2015 Agreements.

The ESSP for the DM1 R&D Services was determined to be $1.7 million, which was based on estimates of the associated effort and cost of the services, adjusted for a reasonable profit margin that would be expected to be realized under similar contracts. On a relative basis, $1.1 million of the initial transaction price was allocated to the DM1 R&D Services.

As discussed above, in December 2021, the Company adjusted the transaction price of the 2019 Collaboration Agreement to include $12.5 million of previously constrained variable consideration associated with a research milestone. The milestone was allocated to the performance obligations using the relative standalone selling price method based on the ESSP's described herein. As a result, revenue of $12.0 million was recognized for amounts allocated to fully satisfied performance obligations. Amounts allocated to unsatisfied performance obligations of $0.5 million were included in deferred revenue.

Recognition of Revenue

The Company determined that the DMD License and DM1 License represent 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. As such, the revenue related to the licenses was recognized at the point in time in which they were delivered during the third quarter of 2019.

The revenue allocated to the waiving of Vertex's material right associated with its option to a fourth exclusive license in connection with Company's reacquisition of exclusive rights to the specified target was recognized at the point in time in which the option was waived, on the effective date of the 2019 Agreements.

The Company concluded that the Specified Target Option and Collaboration Target Options were considered material rights under the Vertex Agreements. Revenue related to the three Collaboration Target Options material right was recognized at the point in time in which Vertex exercised the Collaboration Target Options, which occurred in the fourth quarter of 2019.

The Company recognized revenue related to the DM1 R&D Services over time as the services were rendered, which concluded in the fourth quarter of 2021.

Revenue recognized in connection with the Vertex Agreements

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 CTX001 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.

Revenue recognized under the Vertex Agreements for the year ended December 31, 2019 was $289.1 million. The $289.1 million of revenue recognized for the year-ended December 31, 2019 was comprised of (i) revenue related to the DMD License and DM1 License of $202.4 million, which was recognized at the point in time in which the licenses were delivered, (ii) revenue related to the Collaboration Target Options material right of $76.7 million, which was recognized upon the exercise of the Collaboration Target Options by Vertex and is inclusive of the $30.0 million payment made by Vertex to exercise those options, (iii) revenue allocated to the waiving of Vertex's material right associated with its option to a fourth exclusive license in connection with the Company's reacquisition of exclusive rights to the specified target of $6.7 million, which was recognized at the point in time in which the option was waived, (iv) revenue recognized in connection with DM1 R&D Services of $0.1 million and (v) revenue recognized of $0.1 million related to both research and development services as well as the amortization of the non-exclusive research license under the 2015 Agreements. Additionally, the Company recognized revenue related to 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 the third quarter of 2019.

As of December 31, 2021 and 2020 there was $0.0 million and $0.4 million of current deferred revenue related to the collaboration with Vertex, respectively. As of December 31, 2021 and 2020, there was $12.3 million and $11.8 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 CTX001 program and CTX001 ultimately achieves regulatory approval in such areas, then the Company could be entitled to certain milestone payments aggregating to high eight digits from Vertex.

Each of the remaining milestones are fully constrained as of December 31, 2021. There is uncertainty that the events to obtain the research and developmental milestones will be achieved given the nature of clinical development and the stage of the CRISPR/Cas9 technology. The remaining research, development and regulatory milestones will be constrained until it is probable that a significant revenue reversal will not occur. Commercial milestones and royalties relate predominantly to a license of intellectual property and are determined by sales or usage-based thresholds. The commercial milestones and royalties are accounted for under the royalty recognition constraint and will be accounted for as constrained variable consideration. The Company applies the royalty recognition constraint for each commercial milestone and will not recognize revenue for each until the subsequent sale of a licensed product (achievement of each) occurs.

Accounting Analysis under ASC 808

In connection with the Vertex Agreements, the Company identified the following collaborative elements, which are accounted for under ASC 808: (i) development and commercialization services for shared products, including any transition services related to CTX001 under the A&R JDCA; (ii) R&D Services for follow-on products; and (iii) committee participation. The related impact of the cost sharing associated with research and development is included in research and development expense. Expenses related to services performed by the Company are classified as research and development expense. Payments received from Vertex for partial reimbursement of expenses are recorded as a reduction of research and development expense.

During the years ended December 31, 2021, 2020 and 2019, the Company recognized $111.6 million, $48.6 million, and $29.2 million of research and development expense related to the Vertex Agreements, respectively. Research and development expense for the years ended December 31, 2021, 2020 and 2019 is net of $47.4 million, $28.2 million, and $15.9 million of reimbursements from Vertex, respectively.

Accounting Analysis under ASC 730

In connection with the 2019 Agreements, the Company and Vertex agreed that one of the four remaining options under the 2015 Agreements, as amended, would not be exercised; instead, the Company will conduct research and development activities for a 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 do so within a specified time period, 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 connection therewith, the Company determined that in order for the Company to obtain the right to conduct research and development activities on the specified target, the Company had waived its right to receive an option exercise payment of $10.0 million from Vertex, which was included as non-cash consideration in the transaction price for the 2019 Agreements described above. The Company then subsequently reacquired its rights to the specified target by waiving payment owed by Vertex of $10.0 million for a license that represents in-process research and development and therefore, $10.0 million of non-cash consideration was fully expensed upon the execution of the 2019 Agreements. The Company also determined that research and development services through IND for the specified target and any payment of future development and commercialization milestones, as well as sales-based milestones and royalties for the specified target, would be accounted for as research and development costs under ASC 730 and expensed as incurred. In addition, the Company also determined that should the Company elect its option to co-develop and co-commercialize all DM1 products globally, it will record the option fee as research and development expense upon exercise.

In connection with the A&R Vertex JDCA, Vertex has the option to conduct research at their own cost in certain defined areas that, if beneficial to the CTX001 program and CTX001 ultimately achieves regulatory approval in such areas, then the Company could owe Vertex certain milestone payments aggregating to high eight digits, subject to certain limitations on the profitability of the CTX001 program.

Agreements with Bayer Healthcare LLC

Summary

On December 19, 2015, the Company entered into an agreement with Bayer, to establish a joint venture to focus on the research and the development of new therapeutics to cure blood disorders, blindness and congenital heart disease. On February 12, 2016, the Company and Bayer completed the formation of the joint venture entity, Casebia. Bayer and the Company each received a 50% equity interest in the entity in exchange for their respective contributions to the entity. At that time, the Company also entered into a separate service agreement with Casebia, under which the Company agreed to provide compensated research and development services. Collectively, these agreements are referred to as the "2015 Casebia Agreements."

On December 13, 2019, the Company, Bayer and Casebia entered into a series of transactions by which, among other things, the Company acquired 100% of the partnership interests in Casebia, or the Retirement Agreement, the Company and Bayer terminated their joint venture, or the Joint Venture Termination Agreement, and the Company and Bayer entered into a new option agreement, or the 2019 Option Agreement. Collectively, these agreements are referred to as the "2019 Casebia Agreements."

In connection with the Retirement Agreement, Casebia retired Bayer's outstanding partnership interests in exchange for $22.0 million less certain estimated interim operating expenses of $6.0 million, and the Company acquired 100% of the partnership interests in Casebia.

In connection with entering into the Retirement Agreement, the Company, Bayer and Casebia entered into the Joint Venture Termination Agreement. In connection therewith, the Company and Bayer agreed to terminate the Joint Venture Agreement from December 2015. Under the Joint Venture Termination Agreement, Casebia-owned patents are now co-owned by the Company and Bayer, subject to certain exclusive licenses granted therein. Under the Joint Venture Termination Agreement, the Company and Bayer each retained rights to their respective contributed intellectual property.

In connection with entering into the Retirement Agreement and the Joint Venture Termination Agreement, the Company and Bayer also entered into the 2019 Option Agreement, under which, among other things, the Company committed to invest a specified amount in certain research and development activities as described under "Accounting Analysis – Accounting for 2019 Casebia Agreements". In addition, Bayer has an option (exercisable during a specified exercise period defined by future events, but in no event longer than 5 years after the effective date of the 2019 Option Agreement) to co-develop and co-commercialize two products for the diagnosis, treatment or prevention of certain autoimmune disorders, eye disorders, or hemophilia A disorders. In the event Bayer elects to co-develop and co-commercialize a product, the parties will negotiate and enter into a co-development and co-commercialization agreement, or the Co-Commercialization Agreement, for such product, and Bayer would be responsible for 50% of the research and development costs incurred by the Company for such product going forward. Bayer would receive 50% of all profits from sales of such product and would be responsible for 50% of all losses.

If Bayer elects to exercise its option to co-develop and co-commercialize a product, Bayer will make a one-time $20.0 million payment, or the Option Payment, to the Company that will become non-refundable once the parties execute a Co-Commercialization Agreement with respect to such optioned product. The Option Payment is payable only once with respect to the first time Bayer exercises an option under the 2019 Option Agreement.

In addition, following Bayer's exercise of its option and/or the execution of the Co-Commercialization Agreement for an optioned product, for a period beginning on the effective date of such Co-Commercialization Agreement and ending on the earlier of the three month anniversary of such effective date or during the 90-day negotiation process of such Co-Commercialization Agreement, Bayer has a right to negotiate an exclusive license to develop and commercialize such optioned product. If Bayer exercises such right, the parties will enter into an exclusive license agreement for such optioned product on terms mutually agreeable to the parties. Further, the Option Payment paid for such optioned product would become credited against payments due under such exclusive license or any other exclusive license entered into in connection with the 2019 Option Agreement.

Either party may terminate the 2019 Option Agreement upon the other party's material breach, subject to specified notice and cure provisions. The Company may also terminate the 2019 Option Agreement in the event Bayer commences or participates in any action or proceeding challenging the validity or enforceability of any Company patent necessary or useful for the research, development, manufacture or commercialization of a product that is the subject of the 2019 Option Agreement. Bayer may also terminate the 2019 Option Agreement upon the Company's bankruptcy or insolvency, or for convenience at any time, after giving written notice.

Accounting Analysis

Accounting for the 2015 Casebia Agreements

Transactions under the 2015 Casebia Agreements ceased on the effective date of the 2019 Casebia Agreements. There was no financial impact of the 2015 Casebia Agreements for the years ended December 31, 2021 and 2020.

For the year ended December 31, 2019, the only element of the 2015 Casebia Agreements accounted for in accordance with ASC 808 was the cost sharing activity with Casebia with respect to shared research and technology licenses with other vendors for which the Company determined the arrangement was a cost/profit sharing arrangement and not a revenue arrangement. The related impact of the cost sharing included in R&D expense for the year ended December 31, 2019 was not material. Cost sharing activity ceased with the execution of the 2019 Casebia Agreements.

For the year ended December 31, 2019, the only element of 2015 Casebia Agreements accounted for in accordance with ASC 606 was the obligation to perform research and development services for Casebia. Revenue recognized for research and development was not material for the year ended December 31, 2019. This performance obligation was terminated upon the execution of the 2019 Casebia Agreements.

Loss from Equity Method Investment

During the year ended December 31, 2019, the Company recognized $5.5 million of stock-based compensation expense related to Casebia employees. Unrecognized equity method losses in excess of the Company's equity investment in Casebia was $72.0

million as of December 31, 2019. Total net loss of Casebia for the period ending December 13, 2019 (prior to the Company's consolidation of Casebia) was $58.8 million.

Accounting for the 2019 Casebia Agreements

The Company determined that the Retirement Agreement and Joint Venture Termination Agreement resulted in the Company obtaining a controlling interest in Casebia and should be accounted for as a separate component from the 2019 Option Agreement. In doing so, the Company allocated the consideration transferred of $41.0 million (consisting of $16.0 million of assets acquired net of the purchase price, as displayed in the table below, and $25.0 million of cash allocated to the 2019 Option Agreement) between the two components using a relative fair value approach. The Company determined the relative fair value related to obtaining a controlling interest in Casebia was $32.0 million and the relative fair value of the consideration transferred related to the 2019 Option Agreement was $25.0 million, which is comprised of $20.2 million related to certain research and development activities and $4.8 million related to certain options as described above.

As a result of the Retirement Agreement, the Company determined that it had obtained a controlling interest in a VIE, for which it became the primary beneficiary. As such, under ASC 810, *Consolidation,* the Company accounted for the net assets obtained under ASC 805, *Business Combinations*. In accordance therewith, the Company determined the set of acquired assets and assumed liabilities did not meet the definition of a business, as the Company did not acquire an assembled workforce and thus the Company did not acquire substantive processes capable of producing outputs. As such, no goodwill was recorded. The Company measured the fair value of the assets and liabilities received, determining the relative fair value was $16.0 million (after paying the $16.0 million for Bayer's 50% interest) and recorded the difference between that amount and the Company's carrying amount, which was zero, as a gain within other income (expense). The relative fair value of the assets and liabilities received (exclusive of the $16.0 million paid from Casebia to Bayer to retire Bayer's interest in the JV) was determined as follows (in thousands):

Fair value	Amount
Cash and cash equivalents	$ 6,784
Prepaid expenses and other current assets	2,565
Property, plant and equipment, net	9,340
Operating lease assets	11,003
Restricted cash	1,226
Accrued expenses and other current liabilities	(3,915)
Operating lease liabilities	(11,003)
Net assets	$ 16,000

The value of the reacquired rights related to the intellectual property was determined to be insignificant.

The Company determined that the 2019 Option Agreement should be accounted for under ASC 730-20. This determination was based on the fact that the financial risk associated with the research and development has been transferred to the Company because repayment of any of the funds provided by Bayer depends solely on the results of the research and development having a future economic benefit. The Company further determined that it had two separate obligations under the 2019 Option Agreements, which consist of (i) research and development services and (ii) future delivery of up to two options for products in defined fields. The relative fair value of the obligations was determined to be $20.2 million and $4.8 million, respectively. As the Company has accounted for its obligations as a contract to perform research and development for others, with respect to the obligation to perform research and development services the Company will recognize an offset to research and development expense as the research is performed and, with respect to the future delivery of up to two option for products in defined fields, at the earlier of option exercise (at or near IND application filing), expiration, or when commercially reasonable efforts to progress the program have been exhausted.

During the years ended December 31, 2021 and 2020, the Company recorded a benefit of $7.0 million and $13.2 million to research and development expense for qualifying expenses incurred under the 2019 Option Agreement. As of December 31, 2021, the Company has recorded $4.8 million in other long-term liabilities consisting of the relative fair value of the options, which was unchanged from December 31, 2020. As of December 31, 2020, the Company recorded $7.0 million in other current liabilities relating to certain research and development obligations to be satisfied within one year of the balance sheet date. All research and development obligations under the 2019 Option Agreement were satisfied as of December 31, 2021.

10. Share Capital

The Company had 145,364,335 and 115,172,786 authorized common shares as of December 31, 2021 and 2020, 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**	**2021**	**2020**
Common shares	Registered share capital	80,321,227	75,133,951
Common shares	Authorized share capital	39,316,975	17,625,426
Common shares	Conditional share capital - Bonds or similar debt instruments	4,919,700	4,919,700
Common shares	Conditional share capital - Employee benefit plans	20,806,433	17,493,709
	Total	145,364,335	115,172,786

Included in registered share capital are 5,038,262 shares registered, which are held by the Company and its subsidiaries and are reserved for future issuance for financings.

Common Share Issuances

Recent Public Offerings

In November 2019, the Company sold 4.9 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 $64.50 per share for aggregate net proceeds of $297.4 million, which were net of equity issuance costs of $17.8 million. Additional equity issuance costs of $3.0 million for stamp taxes were also paid in 2019.

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 the first quarter of 2019, the Company began to issue and sell securities under an Open Market Sale Agreement[SM] entered into with Jefferies LLC, or Jefferies, in August 2018, under which the Company was able to offer and sell, from time to time, common shares having aggregate gross proceeds of up to $125.0 million, or the 2018 ATM. During the year ended December 31, 2019, the Company issued and sold an aggregate of 2.8 million common shares at an average price of $44.38 per share for aggregate net proceeds of $120.6 million, which were net of equity issuance costs of $4.4 million. In addition, the Company paid approximately $0.9 million in stamp taxes during the year ended December 31, 2019 and accrued an additional $0.3 million for stamp taxes as of December 31, 2019. The Company paid the $0.3 million for stamp taxes in 2020.

In August 2019, the Company entered into an Open Market Sale Agreement[SM] with 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, or the 2021 ATM. As of December 31, 2021, the Company has issued and sold an aggregate of 1.1 million common shares under the 2021 ATM at an average price of $169.82 per share for aggregate proceeds of $177.8 million, which were net of equity issuance costs of $2.4 million. An additional $1.8 million of stamp taxes related to this amount was paid in 2021.

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, 2021, 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 three years. At December 31, 2021, the Company had 25,005,365 common shares authorized for issuance under the 2018 Plan and 10,298,664 common shares available for future grant under the 2018 Plan.

Equity-Based Compensation Expense

The Company recognized stock-based compensation expense totaling $102.4 million, $66.0 million, and $49.5 million during the years ended December 31, 2021, 2020 and 2019, respectively. Stock-based compensation expense by classification within the consolidated statements of operations and comprehensive income (loss) is as follows (in thousands):

	Years Ended December 31,		
	2021	2020	2019
Research and development	$ 59,683	$ 35,120	$ 23,273
General and administrative	42,707	30,898	20,784
Loss from equity method investment	—	—	5,467
Total	$ 102,390	$ 66,018	$ 49,524

As of December 31, 2021, there was $150.6 million and $71.4 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 2.7 and 2.5 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,		
	2021	2020	2019
Options granted	1,616,255	2,182,773	2,832,784
Weighted-average exercise price	$ 124.32	$ 68.91	$ 39.16
Weighted-average grant date fair value	$ 77.38	$ 42.28	$ 24.57
Assumptions:			
Expected volatility	70.3%	69.2%	68.9%
Expected term (in years)	6.0	6.0	6.0
Risk-free interest rate	1.0%	0.6%	2.2%
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, 2020	8,101,980	$ 42.44	7.8	$ 896,666
Granted	1,616,255	$ 124.32		
Exercised	(1,245,071)	$ 30.96		
Cancelled or forfeited	(660,182)	$ 79.54		
Outstanding at December 31, 2021	7,812,982	$ 58.07	7.4	219,103
Exercisable at December 31, 2021	4,598,353	$ 40.86	6.6	$ 174,056
Vested and expected to vest at December 31, 2021	7,812,982	$ 58.07	7.4	$ 219,103

During 2021 and 2020, the Company did not grant stock option awards subject to performance-based or market-based vesting conditions. As of December 31, 2021, options to purchase 998,504 common shares subject to performance-based vesting conditions were vested, as performance conditions were achieved, and there were 123,057 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.

During 2017, the Company granted 150,000 options with market-based vesting conditions, of which 75% vest at the end of a three-year service period and 25% vest at the end of a four-year service period. Upon achieving a specified average stock price in prior years, the market conditions were satisfied. Expense for the options is being recognized over the requisite service period. As of December 31, 2021, 150,000 of the stock options had vested.

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, 2021, 2020 and 2019 was $119.5 million, $104.2 million, and $42.2 million, respectively.

Restricted Stock

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

	Shares	Weighted-Average Grant Date Fair Value
Unvested balance at December 31, 2020	894,092	$ 70.55
Granted	628,175	111.73
Vested	(455,440)	58.00
Cancelled or forfeited	(132,652)	100.25
Unvested balance at December 31, 2021	934,175	$ 100.14

During the years ended December 31, 2021, 2020 and 2019, the total fair value of restricted stock vested was $45.3 million, $21.6 million, and $3.6 million, respectively.

Award modifications

Equity award modifications for certain equity awards held by departing employees and non-employees for the years ended December 31, 2021, 2020 and 2019 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 21,590 and 13,410 shares under the ESPP during the years ended December 31, 2021 and 2020, respectively.

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

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

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

	Year ended December 31,		
	2021	2020	2019
Net income (loss)	$ 377,661	$ (348,865)	$ 66,858
Basic weighted-average common shares outstanding	75,948,686	65,949,672	54,392,304
Effect of potentially dilutive securities:			
Outstanding options	3,990,579	—	2,406,962
Unvested restricted common shares	454,231	—	133,532
Diluted weighted-average common shares outstanding	80,393,496	65,949,672	56,932,798
Net income (loss) per common share — basic	$ 4.97	$ (5.29)	$ 1.23
Net income (loss) per common share — diluted	$ 4.70	$ (5.29)	$ 1.17

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

	Year ended December 31,		
	2021	2020	2019
Outstanding options	1,765,881	8,101,980	3,789,129
Unvested restricted common shares	225,904	894,092	108,625
ESPP	6,671	11,257	—
Total	1,998,456	9,007,329	3,897,754

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 $3.4 million, $1.9 million, and $1.1 million to the 401(k) Plan for the year ended December 31, 2021, 2020 and 2019, 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 income (loss) before taxes

For the years ended December 31, 2021, 2020 and 2019, the income (loss) before provision for income taxes consist of the following (in thousands):

	Years Ended December 31,		
	2021	2020	2019
Domestic	$ 4,569	$ 7,630	$ 9,155
Foreign	374,962	(355,686)	58,151
Total	$ 379,531	$ (348,056)	$ 67,306

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

	Years Ended December 31,		
	2021	2020	2019
Current income taxes:			
Federal	$ (80)	$ (248)	$ (423)
State	(42)	(151)	(59)
Foreign	—	(1)	0
Total current income taxes	(122)	(400)	(482)
Deferred income taxes:			
Federal	(1,748)	(409)	34
State	—	—	—
Foreign	—	—	—
Total deferred income taxes	(1,748)	(409)	34
Total income tax (provision) benefit	$ (1,870)	$ (809)	$ (448)

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, 2021, 2020 and 2019 is as follows:

	Years Ended December 31,		
	2021	2020	2019
Income tax expense at statutory rate	11.9%	11.9%	9.3%
State income tax, net of federal benefit	(1.0)%	1.0%	(2.1)%
Nondeductible expenses	0.7%	0.1%	(0.1)%
Foreign rate differential	0.6%	(0.1)%	2.0%
Statutory to US GAAP permanent differences	0.0%	0.0%	0.1%
Stock-based compensation	(2.5)%	2.3%	(2.0)%
Impact of deferred rate change	0.0%	0.0%	(12.2)%
Research credits	(4.2)%	3.3%	(5.2)%
Change in valuation allowance	(5.0)%	(18.7)%	10.9%
Effective income tax rate	0.5%	(0.2%)	0.7%

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,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	$ 47,190	$ 84,531
Accruals and reserves	5,878	4,785
Operating lease liabilities	61,476	16,782
Other deferred tax assets	6,362	1,517
Stock-based compensation	14,042	9,605
Deferred revenue	—	86
Research credit	37,878	19,526
Total deferred tax assets	172,826	136,832
Less valuation allowance	(98,649)	(116,640)
Net deferred tax assets	74,177	20,192
Deferred tax liabilities:		
Depreciation	(28,579)	(6,778)
Operating lease assets	(47,521)	(13,776)
Intangible assets	(31)	(31)
Other deferred tax liabilities	(192)	(4)
Total deferred tax liabilities	(76,323)	(20,589)
Long term deferred taxes	$ (2,146)	$ (397)

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, 2021 and 2020, 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 decreased by $18.0 million during 2021, which is primarily attributable to decreases in net operating loss carryforwards as a result of current year net income.

As of December 31, 2021, the Company had available U.S. federal net operating loss carryforwards of $3.3 million. The U.S. federal net operating losses can be carried forward indefinitely. As of December 31, 2021, the Company had available non-U.S. net operating loss carryforwards of $772.9 million of which $385.2 million relate to Switzerland, $385.2 million relate to the Canton of Zug, and $2.5 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, 2021, the Company had U.S. domestic federal research and development credit carryforwards of $19.4 million begin to expire in 2039 for federal purposes, which are net of uncertain tax positions of $9.9 million. As of December 31, 2021, the Company had U.S. domestic federal orphan drug credit carryforwards of $10.6 million which begin to expire in 2040 for federal purposes, which are net of uncertain tax positions of $4.5 million. As of December 31, 2021, the Company had U.S. domestic state research and development credit carryforwards of $10.0 million which begin to expire in 2035, which are net of uncertain tax positions of $7.0 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, 2021, the Company had gross unrecognized tax benefits of $21.4 million of which $19.9 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, 2021, 2020 and 2019, 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,		
	2021	2020	2019
Balance at beginning of year	$ 11,967	$ 5,231	$ 1,595
Increases for tax positions taken during current period	9,911	7,004	2,754
Increases for tax positions taken in prior periods	—	—	882
Decreases for tax positions taken during current period	—	—	—
Decreases for tax positions taken in prior periods	(483)	(268)	—
Balance at end of year	$ 21,395	$ 11,967	$ 5,231

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, 2017. 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.

15. Related Party Transactions

Casebia

Prior to the termination of the joint venture, Casebia was a related party under ASC 850, *Related Party Disclosures* ("ASC 850"). Refer to Note 9, "Agreements with Bayer Healthcare LLC".

Vertex

In the fourth quarter of 2018, upon becoming owners of record of more than 10% of the voting interest of the Company, Vertex became a related party under ASC 850. As of July 2, 2019, upon becoming owners of record of less than 10% of the voting interest of the Company, Vertex was no longer a related party under ASC 850. Refer to Note 9, "Agreements with Vertex Pharmaceuticals Incorporated and certain of its subsidiaries".