UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended June 30, 2020

OR

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

For the transition period from _____ to _____.

Commission File No. 001-36276

ULTRAGENYX PHARMACEUTICAL INC.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization)	**27-2546083** (I.R.S. Employer Identification No.)
60 Leveroni Court **Novato, California** (Address of principal executive offices)	**94949** *(Zip Code)*

(415) 483-8800
(Registrant's telephone number, including area code)

Not Applicable
(Former Name, Former Address and Former Fiscal Year, if Changed Since Last Report)

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

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, $0.001 par value	**RARE**	**The Nasdaq Global Select Market**

As of July 27, 2020, the registrant had 60,589,546 shares of common stock issued and outstanding.

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

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

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

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

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

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

ULTRAGENYX PHARMACEUTICAL INC.

FORM 10-Q FOR THE QUARTER ENDED JUNE 30, 2020

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q (the Quarterly Report) contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Quarterly Report are forward-looking statements. In some cases, you can identify forward-looking statements by words such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or the negative of these words, or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our commercialization, marketing, and manufacturing capabilities and strategy;
- our expectations regarding the timing of clinical study commencements and reporting results from same;
- the timing and likelihood of regulatory approvals for our product candidates;
- the anticipated indications for our product candidates, if approved;
- the potential market opportunities for commercializing our products and product candidates;
- our expectations regarding the potential market size and the size of the patient populations for our products and product candidates, if approved for commercial use;
- the impact of the COVID-19 pandemic and related health measures on our business, financial condition and liquidity;
- estimates of our expenses, revenue, capital requirements, and our needs for additional financing;
- our ability to develop, acquire, and advance product candidates into, and successfully complete, clinical studies;
- the implementation of our business model and strategic plans for our business, products and product candidates and the integration and performance of any businesses we have acquired or may acquire;
- the initiation, timing, progress, and results of ongoing and future preclinical and clinical studies, and our research and development programs;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products and product candidates;
- our ability to maintain and establish collaborations or strategic relationships or obtain additional funding;
- our ability to maintain and establish relationships with third parties, such as contract research organizations, contract manufacturing organizations, suppliers, and distributors;
- our financial performance and the expansion of our organization;
- our ability to obtain supply of our products and product candidates;
- the scalability and commercial viability of our manufacturing methods and processes;
- developments and projections relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under Part II, Item 1A. Risk Factors.

Any forward-looking statements in this Quarterly Report reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those discussed under Part II, Item 1A. Risk Factors and discussed elsewhere in this Quarterly Report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Quarterly Report also contains estimates, projections, and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources.

PART I. FINANCIAL INFORMATION

Item 1. *Financial Statements*

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(Unaudited)
(In thousands, except share amounts)

	June 30, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 335,639	$ 433,584
Short-term investments	477,777	321,646
Receivable related to Daiichi Sankyo license agreements	8,473	—
Accounts receivable, net	14,893	32,844
Inventory	11,061	11,546
Prepaid expenses and other current assets	58,196	51,397
Total current assets	906,039	851,017
Property and equipment, net	48,339	44,348
Investment in Arcturus equity securities	140,220	27,752
Long-term investments	4,068	5,174
Right-of-use assets	37,067	30,328
Intangible assets, net	131,275	129,000
Goodwill	44,406	44,406
Other assets	2,627	3,471
Total assets	$ 1,314,041	$ 1,135,496
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 9,014	$ 12,871
Accrued liabilities	71,887	83,194
Short-term contract liability	131,570	—
Short-term lease liabilities	7,258	7,235
Total current liabilities	219,729	103,300
Long-term contract liability	3,328	—
Long-term lease liabilities	36,308	29,757
Deferred tax liabilities	33,306	33,306
Liability related to the sale of future royalties	325,783	315,369
Total liabilities	618,454	481,732
Stockholders' equity:		
Preferred stock — 25,000,000 shares authorized; nil outstanding as of June 30, 2020 and December 31, 2019	—	—
Common stock — 250,000,000 shares authorized; 60,413,756 and 57,838,220 shares issued and outstanding as of June 30, 2020 and December 31, 2019, respectively	60	58
Additional paid-in capital	2,220,963	2,086,863
Accumulated other comprehensive income (loss)	1,284	(147)
Accumulated deficit	(1,526,720)	(1,433,010)
Total stockholders' equity	695,587	653,764
Total liabilities and stockholders' equity	$ 1,314,041	$ 1,135,496

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(Unaudited)
(In thousands, except share and per share amounts)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Revenues:				
Collaboration and license	$ 50,161	$ 19,247	$ 77,376	$ 33,485
Product sales	8,066	4,902	14,545	8,836
Non-cash collaboration royalty revenue	3,482	—	6,097	—
Total revenues	61,709	24,149	98,018	42,321
Operating expenses:				
Cost of sales	1,803	766	(1,700)	1,218
Research and development	80,709	96,045	193,670	174,150
Selling, general and administrative	42,252	39,812	89,768	78,641
Total operating expenses	124,764	136,623	281,738	254,009
Loss from operations	(63,055)	(112,474)	(183,720)	(211,688)
Interest income	1,797	4,063	4,716	7,149
Change in fair value of investment in Arcturus equity securities	95,200	9,828	102,868	9,828
Non-cash interest expense on liability related to the sale of future royalties	(8,429)	—	(16,511)	—
Other income (expense)	217	(376)	(239)	(788)
Income (loss) before income taxes	25,730	(98,959)	(92,886)	(195,499)
Provision for income taxes	(415)	(213)	(824)	(429)
Net income (loss)	$ 25,315	$ (99,172)	$ (93,710)	$ (195,928)
Net income (loss) per share:				
Basic	$ 0.42	$ (1.72)	$ (1.59)	$ (3.54)
Diluted	$ 0.41	$ (1.72)	$ (1.59)	$ (3.54)
Weighted-average shares used in computing net income (loss) per share:				
Basic	59,995,617	57,519,308	58,996,278	55,376,336
Diluted	61,146,231	57,519,308	58,996,278	55,376,336

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
(Unaudited)
(In thousands)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Net income (loss)	$ 25,315	$ (99,172)	$ (93,710)	$ (195,928)
Other comprehensive income:				
Foreign currency translation adjustments	89	26	40	155
Unrealized gain on available-for-sale securities	2,740	377	1,391	733
Other comprehensive income	2,829	403	1,431	888
Total comprehensive income (loss)	$ 28,144	$ (98,769)	$ (92,279)	$ (195,040)

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(Unaudited)
(In thousands, except share amounts)

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Income (Loss)	Deficit	Equity
Balance as of March 31, 2020	59,488,873	$ 59	$ 2,162,667	$ (1,545)	$ (1,552,035)	$ 609,146
Issuance of common stock in connection with at-the-market offering, net of issuance costs	283,333	—	20,391	—	—	20,391
Employee stock-based compensation	—	—	22,428	—	—	22,428
Issuance of common stock under equity plan awards, net of tax	641,550	1	15,477	—	—	15,478
Other comprehensive income	—	—	—	2,829	—	2,829
Net income	—	—	—	—	25,315	25,315
Balance as of June 30, 2020	60,413,756	$ 60	$ 2,220,963	$ 1,284	$ (1,526,720)	$ 695,587

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Income (Loss)	Deficit	Equity
Balance as of December 31, 2019	57,838,220	$ 58	$ 2,086,863	$ (147)	$ (1,433,010)	$ 653,764
Issuance of common stock in connection with license agreement, net of issuance costs	1,243,913	1	55,267	—	—	55,268
Issuance of common stock in connection with at-the-market offering, net of issuance costs	283,333	—	20,391	—	—	20,391
Employee stock-based compensation	—	—	42,585	—	—	42,585
Issuance of common stock upon exercise of warrants and under equity plan awards, net of tax	1,048,290	1	15,857	—	—	15,858
Other comprehensive income	—	—	—	1,431	—	1,431
Net loss	—	—	—	—	(93,710)	(93,710)
Balance as of June 30, 2020	60,413,756	$ 60	$ 2,220,963	$ 1,284	$ (1,526,720)	$ 695,587

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Income (Loss)	Deficit	Equity
Balance as of March 31, 2019	57,303,888	$ 57	$ 2,013,859	$ (148)	$ (1,127,039)	$ 886,729
Issuance of common stock in connection with at-the-market offering, net of issuance costs	88,978	—	5,523	—	—	5,523
Employee stock-based compensation	—	—	22,490	—	—	22,490
Issuance of common stock under equity plan awards, net of tax	272,509	1	3,813	—	—	3,814
Other comprehensive income	—	—	—	403	—	403
Net loss	—	—	—	—	(99,172)	(99,172)
Balance as of June 30, 2019	57,665,375	$ 58	$ 2,045,685	$ 255	$ (1,226,211)	$ 819,787

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(Unaudited)
(In thousands, except share amounts)

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Income (Loss)	Deficit	Equity
Balance as of December 31, 2018	50,860,588	$ 51	$ 1,639,773	$ (633)	$ (1,030,283)	$ 608,908
Issuance of common stock in connection with underwritten public offering, net of issuance costs	5,833,333	6	330,409	—	—	330,415
Issuance of common stock in connection with at-the-market offering, net of issuance costs	468,685	—	24,828	—	—	24,828
Employee stock-based compensation	—	—	42,960	—	—	42,960
Issuance of common stock under equity plan awards, net of tax	502,769	1	7,715	—	—	7,716
Other comprehensive income	—	—	—	888	—	888
Net loss	—	—	—	—	(195,928)	(195,928)
Balance as of June 30, 2019	57,665,375	$ 58	$ 2,045,685	$ 255	$ (1,226,211)	$ 819,787

See accompanying notes.

ULTRAGENYX PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(Unaudited)
(In thousands)

	Six Months Ended June 30,	
	2020	2019
Operating activities:		
Net loss	$ (93,710)	$ (195,928)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation	42,558	42,428
Amortization of discount on investment securities, net	(149)	(2,960)
Depreciation and amortization	6,036	4,225
Foreign currency remeasurement (gain) loss	25	567
Change in fair value of investment in Arcturus equity securities	(102,868)	(9,828)
Non-cash collaboration royalty revenue	(6,097)	—
Non-cash interest expense on liability related to the sale of future royalties	16,511	—
Other	34	(132)
Changes in operating assets and liabilities:		
Accounts receivable	17,955	(8,161)
Inventory	521	(6,040)
Prepaid expenses and other assets	(6,136)	(3,255)
Receivable related to the Daiichi Sankyo license agreement	(8,473)	—
Right-of-use assets	(6,753)	(17,200)
Accounts payable, accrued, and other liabilities	(8,833)	(7,076)
Contract liabilities	134,898	—
Lease liabilities	6,680	18,522
Net cash used in operating activities	(7,801)	(184,838)
Investing activities:		
Purchase of property and equipment	(18,179)	(8,299)
Purchase of investments	(456,331)	(461,088)
Purchase of investment in Arcturus equity securities	(9,600)	(14,339)
Proceeds from the sale of investments	28,850	22,600
Proceeds from maturities of investments	273,996	301,507
Net cash used in investing activities	(181,264)	(159,619)
Financing activities:		
Proceeds from the issuance of common stock in connection with the license agreement, net	55,268	—
Proceeds from the issuance of common stock in connection with underwritten public offerings, net	—	330,415
Proceeds from the issuance of common stock in connection with at-the-market offering, net	20,391	24,828
Proceeds from the issuance of common stock from exercise of warrants and equity plan awards, net	15,858	7,716
Principal repayments of financing leases	(91)	—
Net cash provided by financing activities	91,426	362,959
Effect of exchange rate changes on cash	(198)	(30)
Net increase (decrease) in cash, cash equivalents and restricted cash	(97,837)	18,472
Cash, cash equivalents and restricted cash at beginning of period	436,244	115,525
Cash, cash equivalents and restricted cash at end of period	$ 338,407	$ 133,997
Supplemental disclosures of non-cash information:		
Acquired lease liabilities arising from obtaining right-of-use assets	$ 3,462	$ 21,515

See accompanying notes.

1. Organization

Ultragenyx Pharmaceutical Inc. (the Company) is a biopharmaceutical company incorporated in California on April 22, 2010. The Company subsequently reincorporated in the state of Delaware in June 2011.

The Company is focused on the identification, acquisition, development, and commercialization of novel products for the treatment of serious rare and ultra-rare genetic diseases. The Company has four approved therapies. Crysvita® (burosumab) is approved in the United States by the U.S. Food and Drug Administration (FDA) and in Canada for the treatment of X-linked hypophosphatemia (XLH) in adult and pediatric patients one year of age and older, and has received European conditional marketing authorization for the treatment of XLH with radiographic evidence of bone disease in children one year of age and older and adolescents with growing skeletons. In Brazil, Crysvita is approved for treatment of XLH in adult and pediatric patients one year of age and older. Crysvita was approved by the FDA on June 18, 2020 for the treatment of FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO), associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adults and pediatric patients 2 years of age and older.

The Company has also received FDA approval for Mepsevii™ (vestronidase alfa), the first medicine approved for the treatment of children and adults with mucopolysaccharidosis VII (MPS VII), also known as Sly syndrome. In the European Union and the United Kingdom, Mepsevii is approved under exceptional circumstances for patients of all ages for the treatment of non-neurological manifestations of MPS VII. In Brazil, Mepsevii is approved for the treatment of MPS VII for patients of all ages.

Dojolvi, formerly known as UX007, was approved by FDA on June 30, 2020 for the treatment of pediatric and adult patients severely affected by long-chain fatty acid oxidation disorders (LC-FAOD).

In addition to the approved treatments, the Company has two ongoing clinical development programs. DTX301 is an adeno-associated virus 8 (AAV8) gene therapy product candidate in development for the treatment of patients with ornithine transcarbamylase (OTC) deficiency, the most common urea cycle disorder; and DTX401 is an AAV8 gene therapy product candidate for the treatment of patients with glycogen storage disease type Ia (GSDIa). The Company operates as one reportable segment.

The Company has sustained operating losses and expects such annual losses to continue over the next several years. The Company's ultimate success depends on the outcome of its research and development and commercialization activities, for which it expects to incur additional losses in the future. Management recognizes that we will likely need to raise additional capital to fully implement its business plans. Through June 30, 2020, the Company has relied primarily on the proceeds from equity offerings and its sale of future royalties to finance its operations.

The Company will likely raise additional capital through the issuance of equity, borrowings, or strategic alliances with partner companies. However, if such financing is not available at adequate levels, the Company would need to reevaluate its operating plans.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited Condensed Consolidated Financial Statements include the accounts of the Company and its wholly-owned subsidiaries and have been prepared in accordance with U.S. generally accepted accounting principles (GAAP) for interim financial information and in accordance with the instructions to Form 10-Q and Rule 10-01 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by GAAP for complete financial statements. The unaudited interim consolidated financial statements have been prepared on the same basis as the annual financial statements. In the opinion of management, the accompanying unaudited Condensed Consolidated financial Statements reflect all adjustments (consisting only of normal recurring adjustments) considered necessary for a fair presentation. These financial statements should be read in conjunction with the audited financial statements and notes thereto for the preceding fiscal year contained in the Company's Annual Report on Form 10-K filed on February 14, 2020 with the United States Securities and Exchange Commission (SEC).

The results of operations for the three and six months ended June 30, 2020 are not necessarily indicative of the results to be expected for the year ending December 31, 2020. The Condensed Consolidated Balance Sheet as of December 31, 2019 has been derived from audited financial statements at that date, but does not include all of the information required by GAAP for complete financial statements.

Use of Estimates

The accompanying consolidated financial statements have been prepared in accordance with GAAP. The preparation of the consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent liabilities and the reported amounts of expenses in the consolidated financial statements and the accompanying notes. On an ongoing basis, management evaluates its estimates, including those related to clinical trial accruals, fair value of assets and liabilities, income taxes, stock-based compensation, and the liability related to the sale of future royalties. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Cash, Cash Equivalents and Restricted Cash

Restricted cash primarily consists of money market accounts as collateral for the Company's obligations under its facility leases. The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the consolidated balance sheets that sum to the total of the same such amounts shown in the consolidated statement of cash flows (in thousands):

	June 30,	
	2020	2019
Cash and cash equivalents	$ 335,639	$ 131,337
Restricted cash included in prepaid expenses and other current assets	847	161
Restricted cash included in other assets	1,921	2,499
Total cash, cash equivalents, and restricted cash shown in the statements of cash flows	$ 338,407	$ 133,997

Credit Losses

Effective January 1, 2020, the Company adopted Accounting Standards Update (ASU) 2016-13, Financial Instruments — Credit Losses, *(Topic 326): Measurement of Credit Losses on Financial Instruments*, which changed the impairment model for most financial assets and certain other instruments. For trade receivables and other instruments, the Company uses a new forward-looking expected loss model that generally results in the earlier recognition of allowances for losses. For available-for-sale debt securities with unrealized losses, the losses are recognized as allowances rather than as reductions in the amortized cost of the securities.

The Company is exposed to credit losses primarily through receivables from customers and collaborators and through its available-for-sale debt securities. The Company's expected loss allowance methodology for the receivables is developed using historical collection experience, current and future economic market conditions, a review of the current aging status and financial condition of the entities. Specific allowance amounts are established to record the appropriate allowance for customers that have a higher probability of default. Balances are written off when determined to be uncollectible. The Company's expected loss allowance methodology for the debt securities is developed by reviewing the extent of the unrealized loss, the size, term, geographical location, and industry of the issuer, the issuers' credit ratings and any changes in those ratings, as well as reviewing current and future economic market conditions and the issuers' current status and financial condition. The Company considered the current and expected future economic and market conditions surrounding the novel coronavirus (COVID-19) pandemic and determined that the estimate of credit losses was not significantly impacted. The adoption of ASU 2016-13 did not have a material impact on the Condensed Consolidated Financial Statements and related disclosures and there was no allowance for losses on available-for-sale debt securities which were attributable to credit risk for the three and six months ended June 30, 2020.

Revenue Recognition

Collaboration and license revenue

The Company has certain license and collaboration agreements that are within the scope of Accounting Standards Codification (ASC) 808, *Collaborative Agreements*, which provides guidance on the presentation and disclosure of collaborative arrangements. Generally, the classification of the transactions under the collaborative arrangements is determined based on the nature of contractual terms of the arrangement, along with the nature of the operations of the participants. The Company records its share of collaboration revenue, net of transfer pricing related to net sales in the period in which such sales occur, if the Company is considered as an agent in the arrangement. The Company is considered an agent when the collaboration partner controls the product before transfer to the customers and has the ability to direct the use of and obtain substantially all of the remaining benefits from the product. Funding received related to research and development services and commercialization costs is generally classified as a reduction of research and development expenses and selling, general and administrative expenses, respectively, in the consolidated statement of operations, because the provision of such services for collaborative partners are not considered to be part of the Company's ongoing major or central operations.

The Company also records royalty revenues under certain of the Company's license or collaboration agreements in exchange for license of intellectual property. If the Company does not have any future performance obligations for these license or collaboration agreements, royalty revenue is recorded as the underlying sales occur.

In order to record collaboration revenue, the Company utilizes certain information from its collaboration partners, including revenue from the sale of the product, associated reserves on revenue, and costs incurred for development and sales activities. For the periods covered in the financial statements presented, there have been no material changes to prior period estimates of revenues and expenses.

The terms of the Company's collaboration and license agreements may contain multiple performance obligations, which may include licenses and research and development activities. The Company evaluates these agreements under ASC 606, *Revenue from Contracts with Customers* (ASC 606), to determine the distinct performance obligations. The Company analogizes to ASC 606 for the accounting for distinct performance obligations for which there is a customer relationship. Prior to recognizing revenue, the Company makes estimates of the transaction price, including variable consideration that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. Total consideration may include nonrefundable upfront license fees, payments for research and development activities, reimbursement of certain third-party costs, payments based upon the achievement of specified milestones, and royalty payments based on product sales derived from the collaboration.

If there are multiple distinct performance obligations, the Company allocates the transaction price to each distinct performance obligation based on its relative standalone selling price. The standalone selling price is generally determined based on the prices charged to customers or using expected cost-plus margin. The Company estimates the efforts needed to complete the performance obligations and recognizes revenue by measuring the progress towards complete satisfaction of the performance obligations using input measures.

Product sales

The Company sells its approved products through a limited number of distributors. Under ASC 606, revenue from product sales is recognized at the point in time when the delivery is made and when title and risk of loss transfers to these distributors. The Company also recognizes revenue from sales of certain products on a "named patient" basis, which are allowed in certain countries prior to the commercial approval of the product. Prior to recognizing revenue, the Company makes estimates of the transaction price, including any variable consideration that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. Product sales are recorded net of estimated government-mandated rebates and chargebacks, estimated product returns, and other deductions.

Provisions for returns and other adjustments are provided for in the period the related revenue is recorded, as estimated by management. These reserves are based on estimates of the amounts earned or to be claimed on the related sales and are reviewed periodically and adjusted as necessary. If actual results vary, the Company may need to adjust these estimates, which could have an effect on earnings in the period of the adjustment.

Non-cash collaboration royalty revenue

Effective January 1, 2020, the Company sold the right to receive certain royalty payments from net sales of Crysvita to RPI Finance Trust (RPI), an affiliate of Royalty Pharma, as further described in Note 7. The Company records the royalty revenue from the net sales of Crysvita in the applicable European territories on a prospective basis as non-cash royalty revenue in the Consolidated Statements of Operations over the term of the arrangement.

3. Financial Instruments

Financial assets and liabilities are recorded at fair value. The carrying amount of certain financial instruments, including cash and cash equivalents, accounts receivable, accounts payable and accrued liabilities approximate fair value due to their relatively short maturities. Assets and liabilities recorded at fair value on a recurring basis in the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2—Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

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

The following tables set forth the fair value of the Company's financial assets remeasured on a recurring basis based on the three-tier fair value hierarchy (in thousands):

	June 30, 2020			
	Level 1	Level 2	Level 3	Total
Money market funds	$ 297,003	$ —	$ —	$ 297,003
Time deposits	—	10,000	—	10,000
Corporate bonds	—	215,486	—	215,486
Commercial paper	—	98,233	—	98,233
Asset-backed securities	—	15,183	—	15,183
U.S. Government Treasury and agency securities	104,924	48,019	—	152,943
Investment in Arcturus equity security	140,220	—	—	140,220
Total	$ 542,147	$ 386,921	$ —	$ 929,068

	December 31, 2019			
	Level 1	Level 2	Level 3	Total
Money market funds	$ 293,309	$ —	$ —	$ 293,309
Repurchase agreements	—	100,000	—	100,000
Time deposits	—	10,000	—	10,000
Corporate bonds	—	77,026	—	77,026
Commercial paper	—	80,119	—	80,119
Asset-backed securities	—	30,406	—	30,406
U.S. Government Treasury and agency securities	96,329	53,979	—	150,308
Investment in Arcturus equity securities	26,088	—	1,664	27,752
Total	$ 415,726	$ 351,530	$ 1,664	$ 768,920

The Company determined the fair value of the Arcturus Therapeutics Holdings Inc. (Arcturus) common stock by using the quoted market price on June 30, 2020, which is a Level 1 fair value measurement.

The fair value of the option to purchase additional shares of Arcturus common stock was based on unobservable inputs that are significant to the measurement of the fair value of the asset and is supported by little or no market data; accordingly, the fair value of the option is considered a Level 3 financial asset. The Company measured the fair value of the option by applying the Black-Scholes option pricing method and utilizing the following inputs: stock price, strike price, volatility, risk-free interest rate, and expected term. The expected term was the Company's estimated period to purchase additional stock. In May 2020, the Company exercised its option to purchase additional shares of Arcturus common stock.

See Note 6 for additional details on the Arcturus transaction.

4. Balance Sheet Components

Cash Equivalents and Investments

The fair values of cash equivalents and investments classified as available-for-sale securities consisted of the following (in thousands):

	June 30, 2020			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Estimated Fair Value
Money market funds	$ 297,003	$ —	$ —	$ 297,003
Time deposits	10,000	—	—	10,000
Corporate bonds	214,224	1,266	(4)	215,486
Commercial paper	98,233	—	—	98,233
Asset-backed securities	15,151	32	—	15,183
U.S. Government Treasury and agency securities	152,687	264	(8)	152,943
Total	$ 787,298	$ 1,562	$ (12)	$ 788,848

	December 31, 2019			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Estimated Fair Value
Money market funds	$ 293,309	$ —	$ —	$ 293,309
Repurchase agreements	100,000	—	—	100,000
Time deposits	10,000	—	—	10,000
Corporate bonds	77,022	17	(13)	77,026
Commercial paper	80,119	—	—	80,119
Asset-backed securities	30,375	31	—	30,406
U.S. Government Treasury and agency securities	150,184	124	—	150,308
Total	$ 741,009	$ 172	$ (13)	$ 741,168

At June 30, 2020, the remaining contractual maturities of available-for-sale securities were less than two years. There have been no realized gains or losses on available-for-sale securities for the three and six months ended June 30, 2020 and 2019. All marketable securities with unrealized losses at June 30, 2020 have been in a loss position for less than twelve months. Based on the Company's application of its expected loss allowance methodology, it is probable that the principal and interest will be collected in accordance with the contractual terms, and that the unrealized loss on these securities were not attributable to credit risk.

Inventory

Inventory consists of the following (in thousands):

	June 30, 2020	December 31, 2019
Work-in-process	$ 7,677	$ 8,191
Finished goods	3,384	3,355
Total inventory	$ 11,061	$ 11,546

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	June 30, 2020	December 31, 2019
Research, clinical study, and manufacturing expenses	$ 21,719	$ 22,894
Payroll and related expenses	35,836	41,324
Other	14,332	18,976
Total accrued liabilities	$ 71,887	$ 83,194

5. Revenue

The following table disaggregates total revenues from customers (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Collaboration and license revenue:				
Crysvita collaboration revenue in profit-share territory	$ 29,806	$ 17,248	$ 57,021	$ 29,187
Royalty revenue in European territory	1,498	1,931	1,498	$ 3,946
Daiichi Sankyo	18,857	—	18,857	—
Bayer	—	68	—	352
Total collaboration and license revenue	50,161	19,247	77,376	33,485
Product sales:				
Crysvita	2,549	1,006	4,159	1,594
Mepsevii	4,185	3,240	7,610	5,913
UX007	1,332	656	2,776	1,329
Total product sales	8,066	4,902	14,545	8,836
Non-cash collaboration royalty revenue	3,482	—	6,097	—
Total revenues	$ 61,709	$ 24,149	$ 98,018	$ 42,321

The following table disaggregates total revenues based on geographic location (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
United States	$ 51,931	$ 20,163	$ 82,288	$ 34,618
Europe	6,548	2,821	10,705	5,732
All other	3,230	1,165	5,025	1,971
Total revenues	$ 61,709	$ 24,149	$ 98,018	$ 42,321

The following table presents changes in the contract assets (liabilities) (in thousands):

	Six Months Ended June 30,	
	2020	2019
Balance of contract assets (liabilities) at beginning of period	$ —	$ 2,979
Additions	(153,755)	352
Deductions	18,857	(3,386)
Balance of contract liabilities at end of period	$ (134,898)	$ (55)

See Note 6 for additional details on contract assets (liabilities) activities.

The Company's largest accounts receivable balance accounted for 79% and 87% of the total accounts receivable balance as of June 30, 2020 and December 31, 2019, respectively, and was due from a collaboration partner.

6. License and Research Agreements

Kyowa Kirin Collaboration and License Agreement

In August 2013, the Company entered into a collaboration and license agreement with Kyowa Kirin Co., Ltd. (KKC or formerly Kyowa Hakko Kirin Co., Ltd. or KHK). Under the terms of this collaboration and license agreement, as amended, the Company and KKC collaborate on the development and commercialization of Crysvita in the field of orphan diseases in the United States and Canada, or the profit-share territory, and in the European Union, United Kingdom, and Switzerland, or the European territory, and the Company has the right to develop and commercialize such products in the field of orphan diseases in Mexico and Central and South America, or Latin America.

Development Activities

In the field of orphan diseases, and except for ongoing studies being conducted by KKC, the Company is the lead party for development activities in the profit-share territory and in the European territory until the applicable transition date; the Company is also the lead party for core development activities conducted in Japan and Korea, for which the core development plan is limited to clinical trials mutually agreed to by the Company and KKC. The Company shares the costs for development activities in the profit-share territory and the European territory conducted pursuant to the development plan before the applicable transition date equally with KKC. KKC is responsible for 100% of the costs for development activities in Japan and Korea. In April 2023, which is the transition date for the profit-share territory, and on the applicable transition date for the European territory, KKC will become the lead party and be responsible for the costs of the development activities. However, the Company will continue to share the costs of the studies commenced prior to the applicable transition date equally with KKC. Crysvita was approved in the European Union and United Kingdom in February 2018 and was approved by the FDA in April 2018.

The collaboration and license agreements are within the scope of ASC 808, which provides guidance on the presentation and disclosure of collaborative arrangements.

Collaboration revenue related to sales in profit-share territory

The Company and KKC share commercial responsibilities and profits in the profit-share territory until April 2023. Under the collaboration agreement, KKC manufactures and supplies Crysvita for commercial use in the profit-share territory and charges the Company the transfer price of 35% of net sales through December 31, 2022, and 30% thereafter. The remaining profit or loss after supply costs from commercializing products in the profit-share territory are shared between the Company and KKC on a 50/50 basis until April 2023. Thereafter, the Company will be entitled to receive a tiered double-digit revenue share in the mid-to-high 20% range.

As KKC is the principal in the sale transaction with the customer, the Company recognizes a pro-rata share of collaboration revenue, net of transfer pricing, in the period the sale occurs. The Company concluded that its portion of KKC's sales in the profit-share territory is analogous to a royalty and therefore recorded its share as collaboration revenue, similar to a royalty.

Royalty revenue related to sales in European territory

KKC has the commercial responsibility for Crysvita in the European territory. In December 2019, the Company sold its right to receive royalty payments based on sales in the European territory to Royalty Pharma, effective January 1, 2020, as further described in Note 7. Prior to the Company's sale of the royalty, the Company received a royalty of up to 10% on net sales in the European territory, which was recognized as the underlying sales occur. Beginning in 2020, the Company records the royalty revenue as non-cash royalty revenues. During the three months ended June 30, 2020, there was a change in estimate of the revenue reserves related to sales made prior to January 1, 2020, as a result of which, the Company recorded $1.5 million as royalty revenue in European territory.

The Company's share of collaboration and royalty revenue related to Crysvita was as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Company's share of revenue in profit-share territory	$ 29,806	$ 17,248	$ 57,021	$ 29,187
Royalty revenue in European territory	1,498	1,931	1,498	3,946
Non-cash royalty revenue in European territory	3,482	—	6,097	—
Total	$ 34,786	$ 19,179	$ 64,616	$ 33,133

Product revenue related to sales in other territories

The Company is responsible for commercializing Crysvita in Latin America and Turkey. The Company is considered the principal in these territories as the Company controls the product before it is transferred to the customer. Accordingly, the Company records revenue on a gross basis related to the sale of Crysvita once the product is delivered and the risk and title of the product is transferred to the distributor. The Company recorded product sales of $2.5 million and $4.2 million for the three and six months ended June 30, 2020, respectively, and $1.0 million and $1.6 million for the three and six months ended June 30, 2019, respectively, net of estimated product returns and other deductions. KKC has the option to assume responsibility for commercialization efforts in Turkey from the Company, after a certain minimum period.

Under the collaboration agreement, KKC manufactures and supplies Crysvita, which is purchased by the Company for sales in the above territories and is based on 35% of the net sales through December 31, 2022 and 30% thereafter. The Company also pays to KKC a low single-digit royalty on net sales in Latin America.

Cost sharing payments

Under the collaboration agreement, KKC and the Company share certain development and commercialization costs. As a result, the Company was reimbursed for these costs and operating expenses were reduced as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Research and development	$ 5,168	$ 5,895	$ 10,658	$ 12,994
Selling, general and administrative	5,965	5,163	13,017	10,376
Total	$ 11,133	$ 11,058	$ 23,675	$ 23,370

Collaboration receivable

The Company had accounts receivable from KKC in the amount of $11.8 million and $28.5 million from profit-share revenue and royalties and other receivables recorded in prepaid and other current assets of $8.2 million and $17.8 million and accrued liabilities of $1.3 million and $0.9 million from commercial and development activity reimbursements, as of June 30, 2020 and December 31, 2019, respectively.

Bayer HealthCare LLC

The Company has an agreement with Bayer Healthcare LLC (Bayer) to research, develop and commercialize AAV gene therapy products for the treatment of hemophilia A (DTX 201). Under this agreement, Bayer has been granted an exclusive license to develop and commercialize one or more novel gene therapies for hemophilia A. The agreement requires that Bayer use commercially reasonable efforts to conduct and fund a proof-of-concept (POC) clinical trial and any subsequent clinical trials and commercialization of gene therapy products for treatment of hemophilia A. Bayer will have worldwide rights to commercialize the potential future product.

Bayer is responsible for funding certain research and development services performed by the Company in the performance of its obligations under the annual research plan and budget. Under the terms of the agreement with Bayer, the Company is eligible to receive development and commercialization milestone payments of up to $232.0 million, as well as, royalty payments ranging in the high single-digit to low double-digit percentages, not exceeding the mid-teens, of net sales of licensed products. The Company achieved the first milestone in December 2017, the second milestone in April 2018, and has received $15.0 million for such milestones to date.

The Company's obligations under the contract were completed by end of December 31, 2019 and as a result, no revenue was recorded for the three and six months ended June 30, 2020. The Company recorded revenue of $0.1 million and $0.4 million for the three and six months ended June 30, 2019, respectively. The Company may record future milestone payments as revenue, if it becomes probable that a significant reversal in the amount of revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved.

Arcturus

The Company has a Research Collaboration and License Agreement with Arcturus to research and develop therapies for select rare diseases. Pursuant to the agreement, the Company incurred $0.4 million and $0.6 million for the three and six months ended June 30, 2019, respectively, in research and development expense for the funding of certain research services received from Arcturus. No research and development expenses were recognized in 2020 related to the Arcturus agreement.

In May 2020, the Company exercised an option to purchase 600,000 shares of Arcturus' common stock at $16.00 per share, or a total purchase price of $9.6 million. Accordingly, after the exercise of the option, the Company owned 3,000,000 shares, or 14.6%, of Arcturus' then outstanding common stock. The purchase was made pursuant to the equity purchase agreement between the parties entered into in June 2019 in connection with the amendment to the research collaboration and license agreement. The Arcturus common stock is restricted from sale or transfer by the Company for six months from the exercise date, subject to certain conditions. The Company has elected to apply the fair value option to account for the equity investment in Arcturus. The Company had accounted for the option to purchase additional shares of Arcturus common stock at fair value based on the Black-Scholes option pricing method.

The changes in the fair value of the Company's investment in Arcturus securities were as follows (in thousands):

	Arcturus common stock	Fair value of option to purchase additional shares of Arcturus common stock	Total
Acquisition of investment in Arcturus securities in June 2019	$ 13,872	$ 467	$ 14,339
Change in fair value	12,216	1,197	13,413
December 31, 2019	26,088	1,664	27,752
Change in fair value	78,920	23,948	102,868
Transfer of value upon option exercise	35,212	(25,612)	9,600
June 30, 2020	$ 140,220	$ —	$ 140,220

GeneTx

In August 2019, the Company entered into a Program Agreement and a Unitholder Option Agreement with GeneTx Biotherapeutics, LLC (GeneTx) to collaborate on the development of GeneTx's GTX-102, an antisense oligonucleotide (ASO) for the treatment of Angelman syndrome.

Pursuant to the terms of the Unitholder Option Agreement, the Company made an upfront payment of $20.0 million for an exclusive option to acquire GeneTx, which was exercisable any time prior to 30 days following FDA acceptance of the IND for GTX-102. Pursuant to the agreement, upon acceptance of IND, the Company elected to extend the option period by paying an option extension payment of $25.0 million (option extension premium) during the prior quarter ended March 31, 2020. The Company has a right to acquire GeneTx for a payment of $125.0 million, at any time, until the earlier of 30 months from the first dosing of a patient in a planned Phase 1/2 study (subject to extensions) or 90 days after results are available from that study. This exclusive option to acquire GeneTx can be extended under certain circumstances, by up to four additional three-month periods, by paying an additional extension fee for each three-month period.

During the exclusive option period, GeneTx is responsible for conducting the program based on the development plan agreed between the parties and, subject to the terms in the Program Agreement, has the decision-making authority on all matters in connection with the research, development, manufacturing and regulatory activities with respect to the Program. The Company will provide support, at its discretion, including strategic guidance and clinical expertise. The Company and GeneTx will collaborate on the submission of the IND and management of the Phase 1/2 study in patients with Angelman syndrome. If the Company acquires GeneTx, the Company will then be responsible for all development and commercialization activities from the date of acquisition. The Company would also be required to make payments upon achievement of certain development and commercial milestones, as well as royalties, depending upon the success of the program.

Although GeneTx is a variable interest entity, the Company is not the primary beneficiary as it currently does not have the power to direct the activities that would most significantly impact the economic performance of GeneTx. Prior to product regulatory approval, all consideration paid to GeneTx represents rights to potential future benefits associated with GeneTx's in-process research and development activities, which have not reached technological feasibility and have no alternative future use. Accordingly, for the three and six months ended June 30, 2020, the Company recorded the option extension payment of none and $25.0 million as an in-process research and development expense.

REGENXBIO, Inc.

In March 2020, the Company executed a License Agreement with REGENXBIO, Inc. (REGENEX), for an exclusive, sublicensable, worldwide license to REGENX's NAV AAV8 and AAV9 Vectors for the development and commercialization of gene therapy treatments for a rare metabolic disorder. In return for these rights, the Company made an upfront payment of $7.0 million, which was recorded as an in-process research and development expense during the prior quarter ended March 31, 2020. The Company will pay certain annual fees of $0.1 million, milestone payments of up to $14.0 million, and royalties on any net sales of products incorporating the licensed intellectual property that range from a high single-digit to low double-digit royalty.

Daiichi Sankyo

In March 2020, the Company executed a License and Technology Access Agreement (the License Agreement) with Daiichi Sankyo Co., Ltd. (Daiichi Sankyo). Pursuant to the License Agreement, the Company granted Daiichi Sankyo a non-exclusive license to intellectual property, including know-how and patent applications, with respect to its HeLa PCL and HEK293 transient transfection manufacturing technology platforms for AAV-based gene therapy products. The Company retains the exclusive right to use the manufacturing technology for its current target indications and additional indications identified now and in the future. The Company will provide certain technical assistance and technology transfer services during the technology transfer period of three years to enable Daiichi Sankyo to use the technologies for its internal gene therapy programs. Daiichi Sankyo has an option to extend the technology transfer period including know-how improvements by two additional one-year periods by paying a fixed amount for each additional year. Daiichi Sankyo will be responsible for the manufacturing, development, and commercialization of products manufactured with the licensed technology; however, the Company has the option to co-develop and co-commercialize rare disease products at the IND stage. Ultragenyx may also provide strategic consultation to Daiichi Sankyo on the development of both AAV-based gene therapy products and other products for rare diseases.

Under the terms of the License Agreement, Daiichi Sankyo made an upfront payment of $125.0 million and will pay an additional $25.0 million upon completion of the technology transfer of the HeLa PCL and HEK293 platforms, as well as single-digit royalties on net sales of products manufactured in either system. Daiichi Sankyo will reimburse the Company for all costs associated with the transfer of the manufacturing technology.

The Company also entered into a Stock Purchase Agreement (SPA) with Daiichi Sankyo, pursuant to which Daiichi Sankyo purchased 1,243,913 shares in exchange for $75.0 million in cash during the first quarter of 2020. The fair market value of the common stock issued to Daiichi Sankyo was $55.3 million based on the stock price of $44.43 on the date of issuance, resulting in a $19.7 million premium on the SPA. Daiichi Sankyo is also subject to a three-year standstill and restrictions on sale of the shares (subject to customary exceptions or release).

In June 2020, the Company executed a subsequent license agreement (the Sublicense Agreement) with Daiichi Sankyo for transfer of certain technology in consideration for an upfront payment of $8.0 million and annual maintenance fees, milestone payments, and royalties on any net sales of products incorporating the licensed intellectual property.

The License Agreement, the Sublicense Agreement, and the SPA are being accounted for as one arrangement because they were entered into at or near the same time and negotiated in contemplation of one another. The Company evaluated the License Agreement and the Sublicense Agreement under ASC 606 and determined that the performance obligations under the agreements are (i) intellectual property with respect to its HeLa PCL and HEK293 transient transfection manufacturing technology platforms together with the initial technical assistance and technology transfer services, which are expected to be completed over a period of 18 months, and (ii) the transfer of any know-how and improvements after the completion of the initial technology transfer through the end of the three year technology transfer period.

The Company determined that the total transaction price of the License Agreement was $183.8 million which was comprised of the $19.7 million premium from the SPA, the $125.0 million upfront payment, the $25.0 million in unconstrained milestone payments, $8.0 million from the Sublicense Agreement, and the $5.5 million estimated reimbursement amount for delivering the license and technology services.

The Company allocated the total transaction price to the two performance obligations on a relative stand-alone selling price basis. Revenue allocated to the intellectual property and the technology transfer services will be recognized over an initial estimated period of 18 to 21 months, measuring the progress toward complete satisfaction of the individual performance obligation using an input measure. Revenue for know-how and improvements after the completion of technology transfer will be recognized over the remaining technology transfer period (i.e., months 19-36) on a straight-line basis, as it is expected that Daiichi Sankyo will receive and consume the benefits consistently throughout the period. The performance obligations are estimated to be substantially complete by March 2023. The estimated period to complete the technology transfer services and the related milestones payments, if any, are subject to revised estimates which could be impacted by limitations or delays from the COVID-19 pandemic, successful scale-up of the manufacturing, and other changes that may impact timing. Royalties from commercial sales will be accounted for as revenue upon achievement of such sales, assuming all other revenue recognition criteria are met.

The technology transfer services were initiated during the second quarter of 2020, as such the Company began recognizing revenue during the period. For the three and six months ended June 30, 2020, the Company recognized $18.9 million in revenue related to this arrangement. Accordingly, the Company had recorded $131.6 million as short-term contract liability and $3.3 million as long- term contract liability as of June 30, 2020. The Company had a receivable related to the above agreements of $8.5 million as of June 30, 2020.

7. Liability Related to the Sale of Future Royalties

In December 2019, the Company entered into a Royalty Purchase Agreement with RPI. Pursuant to the agreement, RPI paid $320.0 million to the Company in consideration for the right to receive royalty payments effective January 1, 2020, arising from the net sales of Crysvita in the European Union, the United Kingdom, and Switzerland under the terms of the Company's Collaboration and License Agreement with KKC dated August 29, 2013, as amended. The agreement with RPI will automatically terminate, and the payment of royalties to RPI will cease, in the event aggregate royalty payments received by RPI are equal to or greater than $608.0 million prior to December 31, 2030, or in the event aggregate royalty payments received by RPI are less than $608.0 million prior to December 31, 2030, when aggregate royalty payments received by RPI are equal to $800.0 million.

As RPI's rate of return is explicitly limited due to the cap on royalties they may receive, proceeds from the transaction were recorded as a liability (liability related to sale of future royalties on the Consolidated Balance Sheets). The Company amortizes $320.0 million, net of transaction cost of $5.8 million using the effective interest method over the estimated life of the arrangement. In order to determine the amortization of the liability, the Company is required to estimate the total amount of future royalty payments to be received by the Company and paid to RPI, subject to the capped amount, over the life of the arrangement. The excess of future estimated royalty payments (subject to the capped amount), over the $314.2 million of net proceeds, is recorded as non-cash interest expense over the life of the arrangement. Consequently, the Company estimates an imputed interest on the unamortized portion of the liability and records interest expense relating to the transaction. The Company records the royalty revenue from the net sales of Crysvita in the applicable European territories as non-cash royalty revenue in the Consolidated Statements of Operations.

The Company periodically assesses the expected royalty payments using a combination of historical results, internal projections and forecasts from external sources. To the extent such payments are greater or less than the Company's initial estimates or the timing of such payments is materially different than its original estimates, the Company will prospectively adjust the amortization of the liability and the effective interest rate. The Company's effective annual interest rate was approximately 10.3% and 10.1% as of June 30, 2020 and December 31, 2019, respectively.

There are a number of factors that could materially affect the amount and timing of royalty payments from KKC in the applicable European territories, most of which are not within the Company's control. Such factors include, but are not limited to, the success of KKC's sales and promotion of Crysvita, changing standards of care, delays or disruptions related to the COVID-19 pandemic, the introduction of competing products, approval of label expansion for adults, pricing for reimbursement in various European territories, manufacturing or other delays, intellectual property matters, adverse events that result in governmental health authority imposed restrictions on the use of Crysvita, significant changes in foreign exchange rates as the royalty payments are made in U.S. dollars (USD) while significant portions of the underlying European sales of Crysvita are made in currencies other than USD, and other events or circumstances that could result in reduced royalty payments from European sales of Crysvita, all of which would result in a reduction of non-cash royalty revenue and the non-cash interest expense over the life of the arrangement. Conversely, if sales of Crysvita in Europe are more than expected, the non-cash royalty revenue and the non-cash interest expense recorded by the Company would be greater over the term of the arrangement.

The following table shows the activity within the liability account (in thousands):

	Liability related to the sale of future royalties
Proceeds from sale of future royalties in December 2019	$ 314,234
Non-cash interest expense	1,135
December 31, 2019	315,369
Non-cash collaboration royalty revenue	(6,097)
Non-cash interest expense	16,511
June 30, 2020	$ 325,783

8. Stock-Based Awards

The 2014 Incentive Plan (the 2014 Plan) provides for automatic annual increases in shares available for grant, beginning on January 1, 2015 through January 1, 2024. As of June 30, 2020, there were 3,304,531 shares reserved under the 2014 Plan for the future issuance of equity awards and 3,287,825 shares reserved for the 2014 Employee Stock Purchase Plan.

The table below sets forth the stock-based compensation expense for the periods presented (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Cost of sales	$ 112	$ 51	$ 180	$ 85
Research and development	12,856	12,032	23,785	23,262
Selling, general and administrative	9,441	10,124	18,616	19,081
Total stock-based compensation expense	$ 22,409	$ 22,207	$ 42,581	$ 42,428

9. Net Income (Loss) Per Share

Basic net income (loss) per share has been computed by dividing the net income (loss) by the weighted-average number of shares of common stock outstanding during the period. Diluted net income (loss) per share is calculated by dividing net income (loss) by the weighted-average number of shares of common stock and potential dilutive securities outstanding during the period. For the six months ended June 30, 2020 and the three and six months ended June 30, 2019, there were no differences between basic and diluted net loss per share since the effect of the dilutive securities would have been antidilutive and therefore were excluded from the diluted net loss per share calculation. The following table sets forth the computation of the basic and diluted net income (loss) per share (in thousands, except share and per share data):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Net income (loss), basic and diluted	$ 25,315	$ (99,172)	$ (93,710)	$ (195,928)
Weighted-average shares used in computing net income (loss) per share, basic	59,995,617	57,519,308	58,996,278	55,376,336
Weighted-average effect of dilutive securities:				
Options to purchase common stock and RSUs	1,150,614	—	—	—
Weighted-average shares used in computing net income (loss) per share, diluted	61,146,231	57,519,308	58,996,278	55,376,336
Net income (loss) per share:				
Basic	$ 0.42	$ (1.72)	$ (1.59)	$ (3.54)
Diluted	$ 0.41	$ (1.72)	$ (1.59)	$ (3.54)

The following weighted-average outstanding common stock equivalents were excluded from the computation of diluted net income (loss) per share for the periods presented because including them would have been antidilutive:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Options to purchase common stock and restricted stock units	5,204,036	8,220,733	8,643,439	7,825,615
Employee stock purchase plan	10,952	7,857	5,476	3,950
Common stock warrants	—	149,700	59,222	149,700
	5,214,988	8,378,290	8,708,137	7,979,265

10. Equity Transactions

In July 2017, the Company entered into an At-The-Market, or ATM, sales agreement with Cowen and Company, LLC (Cowen), whereby the Company could sell up to $150.0 million in aggregate proceeds of common stock from time to time, with Cowen as its sales agent. During the three and six months ended June 30, 2020, the Company sold 283,333 shares of common stock, resulting in net proceeds of $20.4 million, after commissions and other offering costs. During the three and six months ended June 30, 2019, the Company sold 88,978 and 468,685 shares of common stock, respectively, resulting in net proceeds of approximately $5.5 million and $24.8 million, respectively, after commissions and other offering costs. As of June 30, 2020, the Company had completed the sale of all available amounts under the ATM facility.

In February 2019, the Company completed an underwritten public offering in which 5,833,333 shares of common stock were sold, which included 760,869 shares purchased by the underwriters pursuant to an option granted to them in connection with the offering, at a public offering price of $60.00 per share. The total proceeds that the Company received from the offering were approximately $330.4 million, net of underwriting discounts and commissions.

11. Accumulated Other Comprehensive Income (Loss)

Total accumulated other comprehensive income (loss) consisted of the following (in thousands):

	June 30, 2020	December 31, 2019
Foreign currency translation adjustments	$ (266)	$ (306)
Unrealized gain on securities available-for-sale	1,550	159
Total accumulated other comprehensive income (loss)	$ 1,284	$ (147)

Item 2. ***Management's Discussion and Analysis of Financial Condition and Results of Operations***

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with the accompanying unaudited consolidated financial statements and related notes in Item 1 and with the audited consolidated financial statements and the related notes included in our Annual Report on Form 10-K for the year ended December 31, 2019 (the "Annual Report").

Overview

Ultragenyx Pharmaceutical Inc. (we or the Company) is a biopharmaceutical company focused on the identification, acquisition, development, and commercialization of novel products for the treatment of serious rare and ultra-rare genetic diseases. We target diseases for which the unmet medical need is high, the biology for treatment is clear, and for which there are typically no approved therapies treating the underlying disease. Our strategy, which is predicated upon time- and cost-efficient drug development, allows us to pursue multiple programs in parallel with the goal of delivering safe and effective therapies to patients with the utmost urgency.

Impact of COVID-19 Pandemic

The continuing COVID-19 outbreak, which was declared a pandemic by the World Health Organization in March 2020, and the governmental efforts to mitigate the spread of the pandemic, has caused significant volatility and uncertainty in U.S. and international markets and could materially and adversely affect our business and operating results. As with so many other companies throughout the U.S. and globally, our business operations have been and continue to be affected by the COVID-19 pandemic. In addition to some impact on our preclinical manufacturing activities and certain regulatory interactions, we have experienced interruptions to our clinical trial activities, primarily due to delays or disruptions to patient enrollment and dosing as a result of shelter-in-place orders or quarantines, and we anticipate that certain data from our gene therapy product candidates may be delayed as a result of the COVID-19 pandemic. For instance, dosing using prophylactic steroids for our fourth cohort of patients in our Phase 1/2 study for DTX301is currently on hold as a result of COVID-19. Although we have not experienced significant supply interruptions to date, certain of our third-party manufacturers or suppliers have prioritized and allocated more resources and capacity to supply drug product or raw materials to other companies engaged in the study of potential treatments or vaccinations for COVID-19. In response to these events, we are currently seeking alternative sources of supply of drug product or raw materials in an attempt to avoid future potential delays in supply of product, which may result in additional expenses. Social distancing measures and travel limitations in response to the pandemic have also made it difficult for us to identify new patients for our commercialized products, which may result in loss of revenue. We have also restricted access to our facilities to personnel and third parties who perform critical activities that must be performed on-site and as a result, most of our personnel currently work remotely. Such remote working policies may negatively impact productivity and disrupt our business operations.

As the COVID-19 global pandemic continues, we may experience lower revenue and increased expenses as a result of disruptions to our clinical trial, commercialization and regulatory activities, in addition to delays or shortages of drug product and raw materials. The magnitude and extent to which the pandemic may impact our business operations and operating results will continue to remain highly dependent on future developments, which are very uncertain and cannot be predicted with confidence. As a result, we cannot reliably estimate the extent to which the COVID-19 pandemic will impact our financial statements in the second quarter and beyond. See Item 1A: "Risk Factors" for additional details.

Approved Therapies and Clinical Product Candidates

Our current approved therapies and clinical-stage pipeline consist of four product categories: biologics, small molecules, gene therapy, and nucleic acid product candidates.

Our biologic products include approved therapies Crysvita® (burosumab) and Mepsevii® (vestronidase alfa):

- Crysvita is an antibody targeting fibroblast growth factor 23, or FGF23, developed for the treatment of X-linked hypophosphatemia, or XLH, and tumor-induced osteomalacia, or TIO, both of which are disorders characterized by renal phosphate wasting caused by excess FGF23 production. Crysvita is approved in the United States for the treatment of XLH, a rare, hereditary, progressive and lifelong musculoskeletal disorder, in adult and pediatric patients six months of age and older, and in Canada for the treatment of XLH in adult and pediatric patients one year of age and older. In the European Union, or the EU, and the United Kingdom, Crysvita is conditionally approved for the treatment of XLH with radiographic evidence of bone disease in children one year of age and older and adolescents with growing skeletons. On July 24, 2020, the Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion to expand the use of Crysvita for the treatment of XLH in adolescents and adults. This could lead to an expansion of the current market authorization for the treatment XLH in children 1 year of age and older and adolescents with growing skeletons. A formal decision from the European Commission is expected in the second half of 2020. In Brazil, Crysvita is approved for treatment of XLH in adult and pediatric patients one year of age and older. We have submitted regulatory filings in various other Latin American countries.

  Crysvita was approved by the U.S. Food and Drug Administration (FDA) on June 18, 2020 for the treatment of FGF23-related hypophosphatemia in tumor-induced osteomalacia, or TIO, associated with phosphaturic mesenchymal tumors that

cannot be curatively resected or localized in adults and pediatric patients 2 years of age and older. TIO can lead to severe hypophosphatemia, osteomalacia, fractures, fatigue, bone and muscle pain, and muscle weakness.

We are collaborating with Kyowa Kirin Co., Ltd., or KKC (formerly Kyowa Hakko Kirin Co., Ltd., or KHK), and Kyowa Kirin, a wholly owned subsidiary of KKC, on the development and commercialization of Crysvita globally.

- Mepsevii is an intravenous, or IV, enzyme replacement therapy, developed for the treatment of Mucopolysaccharidosis VII, also known as MPS VII or Sly syndrome, a rare lysosomal storage disease that often leads to multi-organ dysfunction, pervasive skeletal disease, and death. Mepsevii is approved in the United States for the treatment of children and adults with MPS VII. In the EU and the United Kingdom, Mepsevii is approved under exceptional circumstances for the treatment of non-neurological manifestations of MPS VII for patients of all ages. In Brazil, Mepsevii is approved for the treatment of MPS VII for patients of all ages.

Our small molecule products include the approved therapy Dojolvi™ (triheptanoin):

- Dojolvi, formerly known as UX007, is a highly purified, synthetic, 7-carbon fatty acid triglyceride specifically designed to provide medium-chain, odd-carbon fatty acids as an energy source and metabolite replacement for people with long-chain fatty acid oxidation disorders, or LC-FAOD, which is a set of rare metabolic diseases that prevents the conversion of fat into energy and can cause low blood sugar, muscle rupture, and heart and liver disease. The FDA approved Dojolvi as a source of calories and fatty acids for the treatment of pediatric and adult patients with molecularly confirmed LC-FAOD on June 30, 2020 and in July 2020, we announced that the product is commercially available in the United States. We have submitted Dojolvi to the Brazilian Health Regulatory Agency (ANVISA) seeking marketing authorization. In Canada, we have been granted priority review have filed a new drug submission. We are also continuing discussions with EU regulatory authorities.

Our gene therapy pipeline includes DTX301 and DTX401 in clinical development for the treatment of two diseases:

- DTX301 is an adeno-associated virus 8, or AAV8 gene therapy product candidate designed for the treatment of patients with ornithine transcarbamylase, or OTC, deficiency. OTC is part of the urea cycle, an enzymatic pathway in the liver that converts excess nitrogen, in the form of ammonia, to urea for excretion. OTC deficiency is the most common urea cycle disorder and leads to increased levels of ammonia. Patients with OTC deficiency suffer from acute hyperammonemic episodes that can lead to hospitalization, adverse cognitive and neurological effects, and death. We estimate that there are approximately 10,000 patients in the developed world with OTC deficiency, of which we estimate approximately 80% are classified as late-onset, our target population. DTX301 has received Orphan Drug Designation in both the United States and in the EU and the United Kingdom and Fast Track Designation in the United States.

  We have reported positive data from the three dose cohorts of the Phase 1/2 study, with six responders of the nine patients dosed in the study and all three patients at the highest dose cohort. A fourth cohort of three patients at the same cohort 3 dose of 1.0 × 10^13 GC/kg is planned using prophylactic steroids. Dosing is delayed due to COVID-19 but we currently expect to release data by the end of 2020.

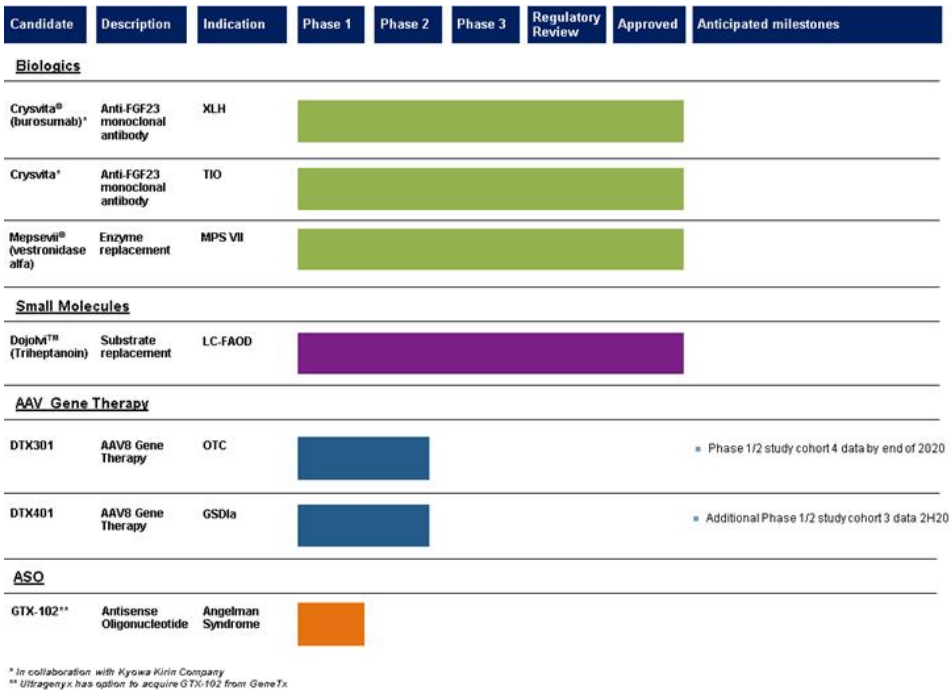
- DTX401 is an AAV8 gene therapy clinical candidate for the treatment of patients with glycogen storage disease type Ia, or GSDIa, a disease that arises from a defect in G6Pase, an essential enzyme in glycogen and glucose metabolism. GSDIa is the most common glycogen storage disease, with an estimated 6,000 patients in the developed world affected by GSDIa. DTX401 has been granted Orphan Drug Designation in both the United States and in the EU and the United Kingdom, Regenerative Medicine Advanced Therapy (RMAT) designation and Fast Track designation in the United States.

  We have reported positive data from three cohorts at two dose levels of the Phase 1/2 study, with all patients showing a clinical response with improvements in glucose control and other metabolic parameters compared to baseline. The confirmatory expansion cohort of three patients at the second cohort dose of 6.0 × 10^12 GC/kg dose is ongoing, and we expect longer-term data to be available from this cohort in the second half of 2020.

Our nucleic acid pipeline includes the option to acquire GTX-102 in clinical development for the treatment of Angelman syndrome:

- GTX-102 is an antisense oligonucleotide, or ASO, that is being developed for the treatment of Angelman syndrome, a debilitating and rare neurogenetic disorder caused by loss-of-function of the maternally inherited allele of the UBE3A gene. There are an estimated 60,000 patients in the developed world affected by Angelman syndrome. GTX-102 was granted Fast Track designation, Orphan Drug Designation and Rare Pediatric Disease Designation from the FDA. GTX-102 is being developed in collaboration with GeneTx Biotherapeutics LLC, or GeneTx. The first two cohorts in the Phase 1/2 study have been fully enrolled with all patients having received multiple doses. Safety and efficacy data from the first two dose escalating cohorts are currently being evaluated and enrollment and dosing at the next dose levels are expected to resume shortly. Preliminary data from the first cohorts of the study are expected in the first half of 2021, provided the COVID-19 pandemic does not cause delays in additional site activation or delays in data collection.

The following table summarizes our approved products and clinical product candidate pipeline:



Recent Clinical Program Updates

Crysvita for the treatment of tumor-induced osteomalacia, or TIO

In June 2020 we and Kyowa Kirin announced the FDA approval of Crysvita for the treatment of fibroblast growth factor 23 (FGF23)-related hypophosphatemia in tumor-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adults and pediatric patients 2 years of age and older.

On July 24, 2020, the CHMP issued a positive opinion to expand the use of Crysvita for the treatment of XLH in adolescents and adults. This could lead to an expansion of the current market authorization for the treatment XLH in children 1 year of age and older and adolescents with growing skeletons. A formal decision from the European Commission is expected in the second half of 2020.

Dojolvi for the treatment of Long-Chain Fatty Acid Oxidation Disorders (LC-FAOD)

In June 2020 we announced the FDA approval of Dojolvi for the treatment of pediatric and adult patients for all forms of LC-FAOD with a molecularly-confirmed diagnosis. Dojolvi is the first FDA-approved therapy for these lifelong and life-threatening genetic disorders. Dojolvi has been submitted for approval with ANVISA in Brazil. In Canada, a new drug submission was filed in July 2020 and Dojolvi has been granted priority review by Health Canada.

DTX301 for the treatment of ornithine transcarbamylase, or OTC, deficiency

In June 2020, we announced updated positive data from the ongoing Phase 1/2 study at the American Society of Gene & Cell Therapy (ASGCT) annual meeting. The updated data confirmed that all three patients in the third dose cohort (1.0 x 10^13 GC/kg) are responders to DTX301 as shown by sustained meaningful increases in the rate of ureagenesis or reductions in ammonia levels. Six of nine patients across all three cohorts have now responded to the gene therapy, including three females and three males. All three

complete responders, those who have discontinued all ammonia scavengers and liberalized their diets, remain clinically and metabolically stable after longer-term follow-up, up to 130 weeks for the longest patient.

A fourth cohort of three patients at the same Cohort 3 dose is planned using prophylactic steroids. Dosing is delayed due to COVID-19 but we currently expect to release data by the end of 2020. We intend to hold an end-of-phase 2 meeting with the FDA based on the first three cohorts, with Phase 3 study initiation currently expected in the first half of 2021.

DTX401 for the treatment of glycogen storage disease type Ia, or GSDIa

In May 2020, we announced positive data from the confirmatory cohort in the ongoing Phase 1/2 study at the ASGCT annual meeting. The data demonstrated increased time to hypoglycemia and substantial reductions in cornstarch usage. Prolonged periods of hyperglycemia were observed in Cohort 3 with the implementation of continuous glucose monitoring (CGM), which is indicative of early transgene expression and glucose release from the liver. The early transgene expression resulted in faster cornstarch reductions in Cohort 3, with a mean reduction of 57% at week 12 compared with 38% and 14% in the first and second cohorts, respectively. Across all three cohorts in the study, 100 percent of patients have demonstrated meaningful and sustained cornstarch regimens over time and significant increases in time to hypoglycemia. After longer-term follow-up, four of six patients in the first two cohorts have discontinued daytime cornstarch.

Additional data on Cohort 3 are expected to be released in the second half of 2020, barring delays related to COVID-19. We also intend to hold an end-of-Phase 2 meeting with the FDA and potentially initiate a Phase 3 study in early 2021, depending on the restrictions and limitations due to COVID-19.

GTX-102 for the treatment of Angelman Syndrome

In May 2020, we announced that the FDA granted Fast Track designation to GTX-102 for the treatment of Angelman syndrome.

Other Developments

Corporate Update

In May 2020, we exercised our option to purchase 600,000 shares of Arcturus' common stock at $16.00 per share; accordingly, after the exercise of the option, we owned 3,000,000 shares of Arcturus' outstanding common stock. The purchase was made pursuant to the equity purchase agreement between the parties entered into in June 2019 in connection with the amendment to the research collaboration and license agreement between the two companies focused on nucleic acid therapies for rare diseases that was initiated in 2015.

Financial Operations Overview

We are a biopharmaceutical company with a limited operating history. To date, we have invested substantially all of our efforts and financial resources in identifying, acquiring, and developing our products and product candidates, including conducting clinical studies and providing selling, general and administrative support for these operations. To date, we have funded our operations primarily from the sale of equity securities and the sale of certain future royalties.

We have incurred net losses in each year since inception. Our net income was $25.3 million for the three months ended June 30, 2020 and our net loss was $93.7 million for the six months ended June 30, 2020, and $99.2 million and $195.9 million for the three and six months ended June 30, 2019, respectively. Net income for the three months ended June 30, 2020 and net loss for the six months ended June 30, 2020 included $95.2 million and $102.9 million, respectively, of changes in fair value of our investment in Arcturus equity securities. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from selling, general and administrative costs associated with our operations.

For the three months ended June 30, 2020, our total revenues increased to $61.7 million, compared to $24.1 million for the same period in 2019 and for the six months ended June 30, 2020, increased to $98.0 million, compared to $42.3 million for the same period in 2019. Revenue for the three and six months ended June 30, 2020 included $18.9 million in revenue from our collaboration and license agreement with Daiichi Sankyo Co., Ltd. (Daiichi Sankyo) which we executed in March 2020. The remainder of the increase was driven by higher revenue from Crysvita collaboration revenue in the profit-share territory, increase in revenue for our approved products and an increase in collaboration royalty revenue.

As of June 30, 2020, we had $817.5 million in available cash, cash equivalents and available-for-sale investments.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the

carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. There have been no material changes in our critical accounting policies during the six months ended June 30, 2020, as compared to those disclosed in "Management's Discussion and Analysis of Financial Condition and Results of Operations — Critical Accounting Policies and Significant Judgments and Estimates" in our Annual Report.

Results of Operations

Comparison of the three and six months ended June 30, 2020 to the three and six months ended June 30, 2019:

Revenue (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2020	2019	Change	Change
Collaboration and license revenue:				
Crysvita collaboration revenue in profit-share territory	$ 29,806	$ 17,248	$ 12,558	73%
Royalty revenue in European territory	1,498	1,931	(433)	-22%
Daiichi Sankyo	18,857	—	18,857	*
Bayer	—	68	(68)	-100%
Total collaboration and license revenue	50,161	19,247	30,914	161%
Product sales:				
Crysvita	2,549	1,006	1,543	153%
Mepsevii	4,185	3,240	945	29%
UX007	1,332	656	676	103%
Total product sales	8,066	4,902	3,164	65%
Non-cash collaboration royalty revenue	3,482	—	3,482	*
Total revenues	$ 61,709	$ 24,149	$ 37,560	156%

* not meaningful

	Six Months Ended June 30,		Dollar	%
	2020	2019	Change	Change
Collaboration and license revenue:				
Crysvita collaboration revenue in profit-share territory	$ 57,021	$ 29,187	$ 27,834	95%
Royalty revenue in European territory	1,498	3,946	(2,448)	-62%
Daiichi Sankyo	18,857	—	18,857	*
Bayer	—	352	(352)	-100%
Total collaboration and license revenue	77,376	33,485	43,891	131%
Product sales:				
Crysvita	4,159	1,594	2,565	161%
Mepsevii	7,610	5,913	1,697	29%
UX007	2,776	1,329	1,447	109%
Total product sales	14,545	8,836	5,709	65%
Non-cash collaboration royalty revenue	6,097	—	6,097	*
Total revenues	$ 98,018	$ 42,321	$ 55,697	132%

For the three months and six months ended June 30, 2020, the Company's share of Crysvita collaboration revenue in the profit-share territory increased by $12.6 million and $27.8 million, respectively, as compared to the same periods in 2019. The increase primarily reflects the continuing increase in demand for Crysvita. In December 2019, we sold the rights to the royalty payments in the European territory, including the United Kingdom and Switzerland, to Royalty Pharma. Beginning in 2020, we record the royalty revenue as non-cash royalty revenues. During the three months ended June 30, 2020, there was a change in estimate of the revenue reserves related to sales made prior to January 1, 2020, as a result, we recorded $1.5 million as royalty revenue in European territory.

In March 2020, we executed a license agreement with Daiichi Sankyo, pursuant to which we granted Daiichi Sankyo a non-exclusive license to intellectual property, including know-how and patent applications, with respect to our HeLa PCL and HEK293 transient transfection manufacturing technology platforms for AAV-based gene therapy products. We will also provide certain technical assistance and technology transfer services during the technology transfer period of three years to enable Daiichi Sankyo to use the technologies for its internal gene therapy programs. For the three and six months ended June 30, 2020, we recognized $18.9 million as collaboration and license revenue from this arrangement. We expect to recognize a substantial majority of the $183.8 million transaction price as revenue over the technology transfer service period, which is currently estimated to be substantially complete by the end of 2021.

The decreases in collaboration and license revenue from our research arrangement with Bayer were due to the transition of the clinical development to Bayer as part of the research arrangement.

The increases in product sales of $3.2 million and $5.7 million for the three and six months ended June 30, 2020, respectively, compared to the same periods in 2019 were primarily due to the continuing increase in demand for our products and increase in sales of certain products under our named patient program in certain countries.

Cost of Sales (dollars in thousands)

	Three Months Ended June 30,		Dollar Change	% Change
	2020	2019		
Cost of sales	$ 1,803	$ 766	$ 1,037	135%

	Six Months Ended June 30,		Dollar Change	% Change
	2020	2019		
Cost of sales	$ (1,700)	$ 1,218	$ (2,918)	-240%

Cost of sales related to our approved products increased by $1.0 million for the three months ended June 30, 2020 and decreased by $2.9 million for the six months ended June 30, 2020, compared to the same periods in 2019. The increase in cost of sales reflect an increase in demand for our approved products. The cost of sales for the six months ended June 30, 2020 included a credit for the manufacturing of future inventory batches with an estimated value of $4.6 million that was agreed to during the period with one of our manufacturers due to certain inventory batches that did not meet specified quality standards. The Company previously recorded reserves of $5.7 million on these inventory batches during the second half of the year ended December 31, 2019, which did not impact cost of sales for the six months ended June 30, 2019.

Prior to the approval of our approved products, manufacturing and related costs were expensed; accordingly, these costs were not capitalized and as a result are not fully reflected in the costs of sales during the current period. If manufacturing and related costs were capitalized prior to the approval period and the credit of $4.6 million as noted above were excluded, we estimate that cost of sales for the three and six months ended June 30, 2020 would have been approximately $1.9 million and $3.1 million, respectively, and for the three and six months ended June 30, 2019 would have been approximately $1.0 million and $1.7 million, respectively, for our commercial product sales. We expect our gross margin percentage to decrease as we produce approved products at costs that reflect the full costs of manufacturing similar to other biologic products and as we deplete inventories that we had expensed prior to receiving FDA approval.

Research and Development Expenses (dollars in thousands)

	Three Months Ended June 30,		Dollar Change	% Change
	2020	2019		
Crysvita	$ 7,427	$ 10,210	$ (2,783)	-27%
Mepsevii	4,208	4,197	11	0%
UX007	9,506	10,407	(901)	-9%
DTX301	8,226	7,722	504	7%
DTX401	3,295	7,581	(4,286)	-57%
GTX102	607	—	607	*
Translational Research	20,670	15,127	5,543	37%
Other research costs	26,770	40,801	(14,031)	-34%
Total research and development expenses	$ 80,709	$ 96,045	$ (15,336)	-16%

	Six Months Ended June 30,		Dollar Change	% Change
	2020	2019		
Crysvita	$ 15,099	$ 20,531	$ (5,432)	-26%
Mepsevii	7,210	9,655	(2,445)	-25%
UX007	19,437	22,775	(3,338)	-15%
DTX301	17,445	19,849	(2,404)	-12%
DTX401	9,899	16,393	(6,494)	-40%
GTX102	26,073	—	26,073	*
Translational Research	47,207	25,017	22,190	89%
Other research costs	51,300	59,930	(8,630)	-14%
Total research and development expenses	$ 193,670	$ 174,150	$ 19,520	11%

Research and development expenses decreased $15.3 million and increased $19.5 million for the three and six months ended June 30, 2020 and 2019, respectively, compared to the same periods in 2019. The changes in research and development expenses was primarily due to:

- for Crysvita, a decrease of $2.8 million and $5.4 million for the three and six months ended June 30, 2020, respectively, primarily related to reduced clinical trial activity with the progressive completion of our extension studies and reduced allocation of employees and contractors to R&D support activities, net of KKC reimbursement;
- for Mepsevii, a nominal increase and a decrease of $2.4 million for the three and six months ended June 30, 2020, respectively, primarily related to reduced clinical trial activity with the progressive completion of our extension studies and reduced allocation of employees and contractors to R&D support activities;
- for UX007, a decrease of $0.9 million and $3.3 million for the three and six months ended June 30, 2020, respectively, primarily related to reduced clinical trial expense for the wind-down of the Glut 1 program, net of increased manufacturing expense due to the timing of drug substance production for the FAOD program;
- for DTX301, an increase of $0.5 million and a decrease of $2.4 million for the three and six months ended June 30, 2020, respectively, primarily related to the timing of clinical drug substance manufacturing activities and drug product batch releases;
- for DTX401, a decrease of $4.3 million and $6.5 million for the three and six months ended June 30, 2020, respectively, primarily related to the timing of clinical drug substance manufacturing activities and drug product batch releases, including a credit for the manufacturing of future batches with an estimated value of $2.9 million that was agreed to during the three months ended June 30, 2020 with one of our manufacturers due to certain batches that did not meet specified quality standards;
- for GTX102, an increase of $0.6 million and $26.1 million for the three and six months ended June 30, 2020, respectively, primarily due to the $25.0 million option extension payment to GeneTx that occurred during the first quarter of 2020;
- for translational research, an increase of $5.5 million and $22.2 million for the three and six months ended June 30, 2020, respectively, related to research, process development, and manufacturing activities, including the progression of our UX701, UX053, and UX068 programs toward IND filings; and during the first quarter of 2020, the $7.0 million payment to REGNEXBIO for exclusive, worldwide rights to NAV AAV8 and AAV9 vectors for the development and commercialization of gene therapy treatments for a rare metabolic disorder;
- for other research and development costs, a decrease of $14.0 million and $8.6 million for the three and six months ended June 30, 2020, respectively, primarily related to the one-time in-process R&D expense of $15.6 million related to the Arcturus Equity Purchase Agreement and amendment to the Research Collaboration and License Agreement incurred in June 2019, net of increases in general operating, facilities, IT, and other overhead expenses in support of our clinical and research program pipeline.

We expect our annual research and development expenses to continue to increase in the future as we advance our product candidates through clinical development. The timing and amount of expenses incurred will depend largely upon the outcomes of current or future clinical studies for our product candidates as well as the related regulatory requirements, manufacturing costs, and any costs associated with the advancement of our preclinical programs.

Selling, General and Administrative Expenses (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2020	2019	Change	Change
Selling, general and administrative	$ 42,252	$ 39,812	$ 2,440	6%

	Six Months Ended June 30,		Dollar	%
	2020	2019	Change	Change
Selling, general and administrative	$ 89,768	$ 78,641	$ 11,127	14%

Selling, general and administrative expenses increased $2.4 million and $11.1 million for the three and six months ended June 30, 2020, respectively, compared to the same periods in 2019. The increases in selling, general and administrative expenses were primarily due to increases in personnel costs resulting from an increase in the number of employees in support of our commercial activities, commercialization costs, and professional services costs.

We expect selling, general and administrative expenses to continue to increase in the future to support our organizational growth and for our expected staged build out of our commercial organization over the next several years related to our approved products and multiple clinical-stage product candidates.

Interest Income (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2020	2019	Change	Change
Interest income	$ 1,797	$ 4,063	$ (2,266)	-56%

	Six Months Ended June 30,		Dollar	%
	2020	2019	Change	Change
Interest income	$ 4,716	$ 7,149	$ (2,433)	-34%

Interest income decreased $2.3 million and $2.4 million for the three and six months ended June 30, 2020, respectively, compared to the same periods in 2019, primarily due to lower portfolio yields as a result of federal reserve interest rate cuts that were made over the past year.

Change in Fair Value of Investment in Arcturus Equity Securities (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2020	2019	Change	Change
Change in fair value of investment in Arcturus equity securities	$ 95,200	$ 9,828	$ 85,372	869%

	Six Months Ended June 30,		Dollar	%
	2020	2019	Change	Change
Change in fair value of investment in Arcturus equity securities	$ 102,868	$ 9,828	$ 93,040	947%

The increases in the fair value of our investment in Arcturus equity securities of $85.4 million and $93.0 million for the three and six months ended June 30, 2020, respectively, were due to the remeasurement to fair value of the Arcturus common stock and the exercise of the option to purchase additional Arcturus stock. Given the historic volatility of the publicly traded stock price of Arcturus, the fair value adjustments of our investments in Arcturus may be subject to wide fluctuations which may have a significant impact on our earnings in future periods. See Item 1A: "Risk Factors" for additional details.

Non-cash Interest Expense on Liability Related to the Sale of Future Royalties (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2020	2019	Change	Change
Non-cash interest expense on liability related to the sale of future royalties	$ (8,429)	$ —	$ (8,429)	*

	Six Months Ended June 30,		Dollar	%
	2020	2019	Change	Change
Non-cash interest expense on liability related to the sale of future royalties	$ (16,511)	$ —	$ (16,511)	*

The non-cash interest expense on liability related to the sale of future royalties of $8.4 million and $16.5 million for the three and six months ended June 30, 2020, respectively, were due to the interest accreted on the liability related to the sale of future royalties for net sales of Crysvita in the European territory pursuant to the Royalty Purchase Agreement entered into with RPI in December 2019. To the extent the royalty payments are greater or less than our initial estimates or the timing of such payments is materially different than our original estimates, we will prospectively adjust the effective interest rate.

Other Income (Expense) (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2020	2019	Change	Change
Other income (expense)	$ 217	$ (376)	$ 593	-158%

	Six Months Ended June 30,		Dollar	%
	2020	2019	Change	Change
Other income (expense)	$ (239)	$ (788)	$ 549	-70%

Other income (expense) increased by $0.6 million and $0.5 million for the three and six months ended June 30, 2020, respectively, compared to the same periods in 2019. The fluctuations were primarily due to fluctuations in foreign exchange rates.

Provision for Income Taxes (dollars in thousands)

	Three Months Ended June 30,		Dollar	%
	2020	2019	Change	Change
Provision for income taxes	$ (415)	$ (213)	$ (202)	95%

	Six Months Ended June 30,		Dollar	%
	2019	2018	Change	Change
Provision for income taxes	$ (824)	$ (429)	$ (395)	92%

The provision for incomes taxes increased by $0.2 million and $0.4 million for the three and six months ended June 30, 2020, respectively, compared to the same periods in 2019. This was primarily due to the increase in commercialization activities in Europe and Latin America.

We are assessing but do not currently anticipate any material impact from the Coronavirus Aid Relief and Economic Security (CARES) Act on our future income tax provisions.

Liquidity and Capital Resources

To date, we have funded our operations primarily from the sale of equity securities and the sale of certain future royalties.

As of June 30, 2020, we had $817.5 million in available cash, cash equivalents, and available-for-sale investments. We believe that our existing capital resources will be sufficient to fund our projected operating requirements for at least the next twelve months. Our cash, cash equivalents, and available-for-sale investments are held in a variety of deposit accounts, interest-bearing accounts, corporate bond securities, U.S government securities, asset-backed securities, and money market funds. Cash in excess of immediate requirements is invested with a view toward liquidity and capital preservation, and we seek to minimize the potential effects of concentration and credit risk.

In February 2019, we completed an underwritten public offering in which we sold 5,833,333 shares of common stock and received net proceeds of approximately $330.4 million. In December 2019, we received net proceeds of $314.2 million from the sale of future royalties to RPI. In March 2020, we received $75.0 million in cash from the sale of 1,243,913 shares of our common stock to Daiichi Sankyo and in April 2020, we received $125.0 million in an upfront payment related to the Daiichi Sankyo License Agreement. During the three and six months ended June 30, 2020, the proceeds from our at-the-market, or ATM, offering were $20.4 million, after commissions and other offering costs. As of June 30, 2020, we had completed the sale of all available amounts under our ATM facility.

The following table summarizes our cash flows for the periods indicated (in thousands):

	Six Months Ended June 30,	
	2020	2019
Cash used in operating activities	$ (7,801)	$ (184,838)
Cash used in investing activities	(181,264)	(159,619)
Cash provided by financing activities	91,426	362,959
Effect of exchange rate changes on cash	(198)	(30)
Net increase (decrease) in cash, cash equivalents and restricted cash	$ (97,837)	$ 18,472

Cash Used in Operating Activities

Our primary use of cash is to fund operating expenses, which consist primarily of research and development and commercial expenditures. Due to our significant research and development expenditures, we have generated significant operating losses since our inception. Cash used to fund operating expenses is affected by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

Cash used in operating activities for the six months ended June 30, 2020 was $7.8 million and reflected a net loss of $93.7 million, $0.1 million for the amortization of the discount paid on purchased investments, $102.9 million for an unrealized gain in the Arcturus equity securities, and $6.1 million for non-cash collaboration royalty revenues related to the sale of future royalties to Royalty Pharma, offset by non-cash charges of $42.6 million for stock-based compensation, $6.0 million for depreciation, and $16.5 million for non-cash interest incurred on the liability related to the sale of future royalties to Royalty Pharma. Cash used in operating activities also reflected a decrease of $6.1 million due to an increase in prepaid expenses and other current assets primarily due to an increase in prepaid manufacturing, a decrease of $8.5 million primarily due to a receivable related to the license agreement with Daiichi Sankyo in June 2020, a $6.8 million decrease due to the addition of the right-of-use assets net of amortization during the period, and a $8.8 million decrease in accounts payable, accrued liabilities, and other liabilities primarily due to a decrease in accrued bonus due to the payout of the 2019 annual bonus, offset by $18.0 million increase due to a decrease in accounts receivable primarily related to change in the timing of billing to a collaboration partner, a $0.5 million increase due to a decrease in inventory, an increase of $134.9 million in contract liabilities related to the license agreements with Daiichi Sankyo, and a $6.7 million increase due to the addition of lease liabilities net of amortization during the period.

Cash used in operating activities for the six months ended June 30, 2019 was $184.8 million and reflected a net loss of $195.9 million, $3.0 million for the amortization of the discount paid on purchased investments, and $9.8 million for an unrealized gain in the Arcturus equity securities, offset by non-cash charges of $42.4 million for stock-based compensation, $4.2 million for depreciation and amortization of an intangible asset acquired, and $0.6 million of non-cash foreign currency remeasurement losses in connection with fluctuations of exchange rates related to intercompany transactions with foreign subsidiaries that are denominated in our reporting currency. Cash used in operating activities also reflected a $8.2 million decrease due to an increase in accounts receivable due to the commercialization of Mepsevii and Crysvita, a $6.0 million decrease due to an increase in inventory as we build out our commercial inventory supplies as we commercialize Mepsevii, a decrease of $3.3 million due to an increase in prepaid expenses and other assets primarily due to an increase in general receivables, amounts due from a collaboration partner, and amounts owed for a tenant improvement allowance, a $17.2 million decrease due to the addition of the right-of-use assets net of amortization during the period, a $7.1 million decrease in accounts payable, accrued expenses, and other liabilities primarily due to a decrease in accrued bonus due to the payout of the 2018 annual bonus, the derecognition of deferred rent obligations for the new lease accounting guidance, and accrued expenses due to the timing of the receipt of invoices, offset by a $18.5 million increase due to the addition of lease liabilities net of amortization during the period.

Cash Used in Investing Activities

Cash used in investing activities for the six months ended June 30, 2020 was $181.3 million and related to purchases of property and equipment of $18.2 million, purchases of investments of $456.3 million, and the exercise of the option to purchase additional Arcturus shares for $9.6 million, offset by proceeds from the sale of investments of $28.9 million and maturities of investments of $274.0 million.

Cash used in investing activities for the six months ended June 30, 2019 was $159.6 million and related to purchases of property and equipment of $8.3 million, purchases of investments of $461.1 million, and purchases of Arcturus equity securities of $14.3 million, offset by proceeds from the sale of investments of $22.6 million and maturities of investments of $301.5 million.

Cash Provided by Financing Activities

Cash provided by financing activities for the six months ended June 30, 2020 was $91.4 million and was comprised of $55.3 million from the sale of common stock in connection with the license agreement with Daiichi Sankyo in March 2020, $20.4 million in net proceeds from the sale of common stock in our ATM offering, and $15.9 million in net proceeds from the issuance of common stock pursuant to the exercise of warrants and equity plan awards, offset by $0.1 million in principal repayments of finance leases.

Cash provided by financing activities for the six months ended June 30, 2019 was $363.0 million and was comprised of $330.4 million from the sale of common stock in our underwritten public offering in February 2019, $24.8 million from the sale of common stock in our ATM offering, and $7.7 million in net proceeds from the issuance of common stock pursuant to equity awards.

Funding Requirements

We anticipate that, excluding non-recurring items, we will continue to generate annual losses for the foreseeable future as we continue the development of, and seek regulatory approvals for, our product candidates, and continue with commercialization of approved products. We will likely require additional capital to fund our operations, to complete our ongoing and planned clinical studies, to commercialize our products, to continue investing in early-stage research capabilities to promote our pipeline growth, to continue to acquire or invest in businesses or products that complement or expand our business, and to further develop our general infrastructure, including building our own Good Manufacturing Practices, or GMP gene therapy manufacturing facility, and such funding may not be available to us on acceptable terms or at all.

If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may be required to delay, limit, reduce the scope of, or terminate one or more of our clinical studies, research and development programs, future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our future funding requirements will depend on many factors, including the following:

- the scope, rate of progress, results and cost of our clinical studies, nonclinical testing, and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates, products that we have begun to commercialize, and any products that we may develop in the future, including the potential development of our own GMP gene therapy manufacturing plant;
- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;

- the cost and timing of establishing our commercial infrastructure, and distribution capabilities;
- the magnitude and extent to which the COVID-19 pandemic impacts our business operations and operating results, as described in “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Risk Factors – Risks Related to Our Business Operations”; and
- the terms and timing of any collaborative, licensing, marketing, distribution, acquisition (including whether we exercise our option to acquire GeneTx pursuant to the terms of our Unitholder Option Agreement with them) and other arrangements that we may establish, including any required upfront milestone, royalty, reimbursements or other payments thereunder.

We expect to satisfy future cash needs through existing capital balances and through some combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, and other marketing and distribution arrangements. Please see “Risk Factors—Risks Related to Our Financial Condition and Capital Requirements.”

Contractual Obligations and Commitments

We have contractual obligations from our operating and finance leases, manufacturing and service contracts, licenses, royalties, development and collaboration arrangements, and other research and development activities. The following table summarizes our significant binding contractual obligations at June 30, 2020 (in thousands):

	Payments due by period				
	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years	Total
Operating and finance leases	$ 10,338	$ 20,917	$ 16,924	$ 6,051	$ 54,230
Manufacturing and service contracts	7,579	49	—	—	7,628
Total	$ 17,917	$ 20,966	$ 16,924	$ 6,051	$ 61,858

The terms of certain of our licenses, royalties, development and collaboration agreements, as well as other research and development activities, require us to pay potential future milestone payments based on product development success. The above table excludes such obligations as the amount and timing of such obligations are unknown or uncertain.

Off-Balance Sheet Arrangements

We have not engaged in any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Item 3. *Quantitative and Qualitative Disclosures about Market Risk*

Equity Risk

We have exposure to equity risk with respect to the equity securities that we hold in Arcturus. The carrying value of our investment in common stock and the option to purchase additional equity securities in Arcturus was $140.2 million and none, respectively, as of June 30, 2020, and $26.1 million and $1.7 million, respectively, as of December 31, 2019. If the Arcturus stock price had been lower at June 30, 2020 compared to December 31, 2019, we may have reported a net loss for the quarter and an even greater net loss for the six months ended June 30, 2020. Given the historic volatility of the publicly traded stock price of Arcturus, the fair value of our investments in Arcturus may be subject to wide fluctuations which may have a significant impact on our earnings in future periods. See Item 1A: "Risk Factors" for additional details.

Interest Rate Risk

Our exposure to market risk for changes in interest rates relates primarily to interest earned on our cash equivalents and investments. The primary objective of our investment activities is to preserve our capital to fund operations. A secondary objective is to maximize income from our investments without assuming significant risk. Our investment policy provides for investments in low-risk, investment-grade debt instruments. As of June 30, 2020, we had cash, cash equivalents, and investments totaling $817.5 million, compared to $760.4 million as of December 31, 2019, which include bank deposits, money market funds, U.S. government treasury and agency securities, and investment-grade corporate bond securities which are subject to default, changes in credit rating, and changes in market value. The securities in our investment portfolio are classified as available for sale and are subject to interest rate risk and will decrease in value if market interest rates increase. Due to the COVID-19 pandemic and the reduction of rates by the U.S. Federal Reserve, we expect that the interest yield on our investments will decrease. A hypothetical 100 basis point change in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements. To date, we have not experienced a loss of principal on any of our investments and as of June 30, 2020, we did not record any allowance for credit loss from our investments.

Foreign Currency Risk

We face foreign exchange risk as a result of entering into transactions denominated in currencies other than U.S. dollars. Due to the uncertain timing of expected payments in foreign currencies, we do not utilize any forward exchange contracts. All foreign transactions settle on the applicable spot exchange basis at the time such payments are made. Volatile market conditions arising from the COVID-19 pandemic may result in significant changes in exchange rates, and in particular a weakening of foreign currencies relative to the U.S. dollar may negatively affect our revenue and operating income as expressed in U.S. dollars. An adverse movement in foreign exchange rates could have a material effect on payments made to foreign suppliers and for license agreements. For the six months ended June 30, 2020, a majority of our revenue and expense activities and capital expenditures were denominated in U.S. dollars. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of our "disclosure controls and procedures" as of the end of the period covered by this Quarterly Report, pursuant to Rules 13a-15(b) and 15d-15(b) under the Securities Exchange Act of 1934, or the Exchange Act. In connection with that evaluation, our Chief Executive Officer and our Chief Financial Officer concluded that our disclosure controls and procedures were effective and designed to provide reasonable assurance that the information required to be disclosed is recorded, processed, summarized and reported within the time periods specified in the SEC rules and forms as of June 30, 2020. For the purpose of this review, disclosure controls and procedures means controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. These disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit is accumulated and communicated to management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, our management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during our first quarter ended June 30, 2020, that has materially affected, or is reasonably likely to materially affect our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1. *Legal Proceedings*

We are not currently a party to any material legal proceedings. We may, however, in the ordinary course of business face various claims brought by third parties or government regulators and we may, from time to time, make claims or take legal actions to assert our rights, including claims relating to our directors, officers, stockholders, intellectual property rights, employment matters and the safety or efficacy of our products. Any of these claims could subject us to costly litigation and, while we generally believe that we have adequate insurance to cover many different types of liabilities, our insurance carriers may deny coverage, may be inadequately capitalized to pay on valid claims, or our policy limits may be inadequate to fully satisfy any damage awards or settlements. If this were to happen, the payment of any such awards could have a material adverse effect on our consolidated operations, cash flows and financial position. Additionally, any such claims, whether or not successful, could damage our reputation and business.

Item 1A. *Risk Factors*

Investing in our common stock involves a high degree of risk. You should carefully consider the following risks, together with all the other information in this Quarterly Report, including our financial statements and notes thereto, before deciding to invest in our common stock. If any of the following risks actually materialize, our operating results, financial condition, and liquidity could be materially adversely affected. As a result, the trading price of our common stock could decline and you could lose part or all of your investment.

The following description of the risk factors associated with our business includes any material changes to and supersedes the description of the risk factors associated with our business previously disclosed in Part I, Item 1A of the Annual Report.

Risks Related to Our Financial Condition and Capital Requirements

We have a history of operating losses and anticipate that we will continue to incur losses for the foreseeable future.

We are a biopharmaceutical company with a history of operating losses, and anticipate continuing to incur operating losses for the foreseeable future. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We have devoted substantially all of our financial resources to identifying, acquiring, and developing our products and product candidates, including conducting clinical studies, developing manufacturing processes, manufacturing product candidates for clinical studies, and providing selling, general and administrative support for these operations. The amount of our future net losses will depend, in part, on non-recurring events, the success of our commercialization efforts, and the rate of our future expenditures. We anticipate that our expenses will increase substantially if and as we:

- continue our research and nonclinical and clinical development of our product candidates;
- expand the scope of our current clinical studies for our product candidates;
- advance our programs into more expensive clinical studies;
- initiate additional nonclinical, clinical, or other studies for our product candidates;
- pursue preclinical and clinical development for additional indications for existing products and product candidates;
- change or add additional manufacturers or suppliers;
- seek to expand upon or build our own manufacturing-related facilities and capabilities, including our plan to build our own GMP gene therapy manufacturing plant;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies;
- continue to establish Medical Affairs field teams to initiate relevant disease education;
- continue to establish a marketing and distribution infrastructure and field force to commercialize our products and any product candidates for which we may obtain marketing approval;
- continue to manage our international subsidiaries and establish new ones;
- continue to operate as a public company and comply with legal, accounting and other regulatory requirements;
- seek to identify, assess, license, acquire, and/or develop other product candidates, technologies, and/or businesses;
- make milestone or other payments under any license or other agreements;
- seek to maintain, protect, and expand our intellectual property portfolio;
- seek to attract and retain skilled personnel;
- create additional infrastructure, including facilities and systems, to support the growth of our operations, our product development, and our commercialization efforts; and
- experience any delays or encounter issues with any of the above, including, but not limited to, failed studies, complex results, safety issues, inspection outcomes, or other regulatory challenges that require longer follow-up of existing studies, additional major studies, or additional supportive studies in order to pursue marketing approval.

The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We have limited experience in revenue from product sales.

Our ability to generate significant revenue from product sales depends on our ability, alone or with strategic collaboration partners, to successfully commercialize our products and to complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize, one or more of our product candidates. Our ability to generate substantial future revenue from product sales, including named patient sales, depends heavily on our success in many areas, including, but not limited to:

- obtaining regulatory and marketing approvals with broad indications for product candidates for which we complete clinical studies;
- developing a sustainable and scalable manufacturing process for our products and any approved product candidates and establishing and maintaining supply and manufacturing relationships with third parties that can conduct the processes and provide adequate (in amount and quality) product supply to support market demand for our products and product candidates, if approved;
- launching and commercializing our products and product candidates for which we obtain regulatory and marketing approval, either directly or with a collaborator or distributor;
- obtaining market acceptance of our products and product candidates as viable treatment options;

- obtaining adequate market share, reimbursement and pricing for our products and product candidates;
- our ability to sell our products and product candidates on a named patient basis or through an equivalent mechanism and the amount of revenue generated from such sales;
- our ability to find patients so they can be diagnosed and begin receiving treatment;
- addressing any competing technological and market developments;
- negotiating favorable terms, including commercial rights, in any collaboration, licensing, or other arrangements into which we may enter, any amendments thereto or extensions thereof;
- maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

If the number of our addressable rare disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice, or treatment guidelines, we may not generate significant revenue from sales of our products, even if they receive regulatory approval.

We expect we will likely need to raise additional capital to fund our activities. This additional financing may not be available on acceptable terms, if at all. Failure to obtain this necessary capital when needed may force us to delay, limit, or terminate our product development efforts or other activities.

As of June 30, 2020, our available cash, cash equivalents, and investments were $817.5 million. We expect we will likely need additional capital to continue to commercialize our products, and to develop and obtain regulatory approval for, and to commercialize, all of our product candidates. In addition, our operating plans may change as a result of many factors that may currently be unknown to us, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including but not limited to:

- the scope, rate of progress, results, and cost of our clinical studies, nonclinical testing, and other related activities;
- the cost of manufacturing clinical and commercial supplies of our products and product candidates;
- the cost of creating additional infrastructure, including facilities and systems;
- the number and characteristics of the product candidates that we pursue;
- the cost, timing, and outcomes of regulatory approvals;
- the cost and timing of establishing and operating our international subsidiaries;
- the cost and timing of establishing and operating field forces, marketing, and distribution capabilities;
- the cost and timing of other activities needed to commercialize our products; and
- the terms and timing of any collaborative, licensing, acquisition (including whether we exercise our option to acquire GeneTx pursuant to the terms of our Unitholder Option Agreement with them), and other arrangements that we may establish, including any required milestone, royalty, and reimbursements or other payments thereunder.

Any additional fundraising efforts may divert our management's attention from their day-to-day activities, which may adversely affect our ability to develop our product candidates and commercialize our products. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. The terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. If we incur debt, it could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell, or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. We have in the past sought and may in the future seek funds through a sale of future royalty payments similar to our transaction with Royalty Pharma or through collaborative partnerships, strategic alliances, and licensing or other arrangements, such as our transaction with Daiichi Sankyo, and we may be required to relinquish rights to some of our technologies or product candidates, future revenue streams, research programs, and other product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results, and prospects. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

In addition, as a result of the COVID-19 pandemic, the stock market in general and the stock price of biopharmaceutical companies, in particular, have experienced extreme price and volume fluctuations. As a result of such volatility and the impact of the COVID-19 pandemic on financial markets in general, our access to and cost of capital may be negatively affected.

If we are unable to obtain funding on a timely basis or at all, we may be required to significantly curtail, delay, or discontinue one or more of our research or development programs or the commercialization of our products and any approved product candidates or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition, and results of operations.

Risks Related to the Discovery and Development of Our Product Candidates

Clinical drug development involves a lengthy and expensive process with uncertain outcomes and the potential for substantial delays, and the results of earlier studies may not be predictive of future study results.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, time consuming, and uncertain as to outcome. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical studies can occur at any stage of testing, and our future clinical studies may not be successful. Product candidates that have shown promising results in early-stage clinical studies may still suffer significant setbacks in subsequent clinical studies. The safety or efficacy results generated to date in clinical studies do not ensure that later clinical studies will demonstrate similar results. For example, our Phase 3 studies that evaluated Ace-ER in patients with GNE myopathy and UX007 in patients with Glut1 DS experiencing disabling paroxysmal movement disorders did not achieve their primary or secondary endpoints. Results from investigator-sponsored studies or compassionate-use studies may not be confirmed in company-sponsored studies or may negatively impact the prospects for our programs. Additionally, given the nature of the rare diseases we are seeking to treat, we often have to devise newly-defined endpoints to be tested in our studies, which can lead to some subjectivity in interpreting study results and could result in regulatory agencies not agreeing with the validity of our endpoints, or our interpretation of the clinical data, and therefore denying approval. Given the illness of the patients in our studies and the nature of their rare diseases, we may also be required or choose to conduct certain studies on an open-label basis. We have in the past, and may in the future elect to review interim clinical data at multiple time points during the studies, which could introduce bias into the study results and potentially result in denial of approval.

In the biopharmaceutical industry, there is a high failure rate for drugs and biologics proceeding through clinical studies, and product candidates in later stages of clinical studies may fail to show the desired safety and efficacy despite having progressed through nonclinical studies and initial clinical studies. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical studies due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies.

Scenarios that may prevent successful or timely completion of clinical development include but are not limited to:

- delays or failures in generating sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of human clinical studies or filings for regulatory approval;
- failure to demonstrate a starting dose for our product candidates in the clinic that might be reasonably expected to result in a clinical benefit;
- delays or failures in developing gene therapy, messenger RNA (mRNA), DNA, small interfering RNA (siRNA) or other novel and complex product candidates, which are expensive and difficult to develop and manufacture;
- delays resulting from a shutdown, or uncertainty surrounding the potential for future shutdowns of the U.S. government, including the FDA;
- delays or failures in reaching a consensus with regulatory agencies on study design;
- delays in reaching agreement on acceptable terms with contract research organizations, or CROs, clinical study sites, and other clinical trial-related vendors;
- failure or delays in obtaining required regulatory agency approval and/or IRB or EC approval at each clinical study site or in certain countries;
- failure to correctly design clinical studies which may result in those studies failing to meet their endpoints or the expectations of regulatory agencies;
- changes in clinical study design or development strategy resulting in delays related to obtaining approvals from IRBs or ECs and/or regulatory agencies to proceed with clinical studies;
- imposition of a clinical hold by regulatory agencies after review of an IND application or amendment, another equivalent application or amendment, or an inspection of our clinical study operations or study sites;
- delays in recruiting suitable patients to participate in our clinical studies;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, other third parties, or us to adhere to clinical study requirements;

- failure to perform in accordance with the FDA's and/or ICH's good clinical practices requirements or applicable regulatory guidelines in other countries;
- delays in patients' completion of studies or their returns for post-treatment follow-up;
- patients dropping out of a study;
- adverse events associated with the product candidate occurring that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- greater than anticipated costs associated with clinical studies of our drug candidates;
- clinical studies of our drug candidates producing negative or inconclusive results, which may result in us deciding, or regulators requiring us, to conduct additional clinical or nonclinical studies or to abandon drug development programs;
- competing clinical studies of potential alternative product candidates or investigator-sponsored studies of our product candidates; and
- delays in manufacturing, testing, releasing, validating, or importing/exporting sufficient stable quantities of our product candidates for use in clinical studies or the inability to do any of the foregoing.

Any inability to successfully complete nonclinical and clinical development could result in additional costs to us or negatively impact our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional toxicology, comparability or other studies to bridge our modified product candidates to earlier versions. Clinical study delays could also shorten any periods during which our products have commercial exclusivity and may allow our competitors to bring products to market before we do, which could negatively impact our ability to obtain orphan exclusivity and to successfully commercialize our product candidates and may harm our business and results of operations.

If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory, and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials, the timing of patient dosing, the submission or acceptance of regulatory filings, and the potential approval of such regulatory filings. We periodically make public announcements about the expected timing of some of these milestones. All of these milestones are based on a variety of assumptions, but the actual timing of these milestones can vary dramatically from our estimates. If we do not meet these publicly announced milestones, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

We may find it difficult to identify and enroll patients in our clinical studies given the limited number of patients who have the diseases for which our product candidates are being studied. Difficulty in enrolling patients could delay or prevent clinical studies of our product candidates.

Identifying and qualifying patients to participate in clinical studies of our product candidates is critical to our success. The timing of our clinical studies depends in part on the speed at which we can recruit patients to participate in testing our product candidates, and we may experience delays in our clinical studies if we encounter difficulties in enrollment.

Each of the conditions for which we plan to evaluate our current product candidates is a rare genetic disease. Accordingly, there are limited patient pools from which to draw for clinical studies. For example,

- we estimate that approximately 8,000 patients in the developed world suffer from late-onset OTC deficiency, for which DTX301 is being studied, and these all may not be treatable if they are immune to the virus; and
- we estimate that approximately 6,000 patients worldwide suffer from GSDIa, for which DTX401 is being studied, and these all may not be treatable if they are immune to the virus.

In addition to the rarity of these diseases, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require patients to have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study. The process of finding and diagnosing patients may prove costly, especially since the rare diseases we are studying are commonly under diagnosed. We also may not be able to identify, recruit, and enroll a sufficient number of appropriate patients to complete our clinical studies because of demographic criteria for prospective patients, the perceived risks and benefits of the product candidate under study, the proximity and availability of clinical study sites for prospective patients, and the patient referral practices of physicians. The availability and efficacy of competing therapies and clinical studies can also adversely impact enrollment. If patients are unwilling to participate in our studies for any reason, the timeline for recruiting patients, conducting studies, and obtaining regulatory approval of potential products may be delayed, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenue from any of these product candidates could be delayed or prevented. Furthermore, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may also ultimately lead to the denial of regulatory approval of our product candidates. Delays in completing our clinical studies will increase our costs, slow down our product candidate development and approval process, and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition, and prospects significantly.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming, and inherently unpredictable. Even if we achieve positive results in our pre-clinical and clinical studies, if we are ultimately unable to obtain timely regulatory approval for our product candidates, our business will be substantially harmed.

Our future success is dependent on our ability to successfully commercialize our products and develop, obtain regulatory approval for, and then successfully commercialize one or more product candidates. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities. We have only obtained regulatory approval for two products, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

To obtain regulatory approval in the United States and other jurisdictions, we must comply with numerous and varying requirements regarding safety, efficacy, chemistry, manufacturing and controls, clinical studies (including good clinical practices), commercial sales, pricing, and distribution of our product candidates. Even if we are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdictions. In addition, approval policies, regulations, positions of the regulatory agencies on study design and/or endpoints, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development, which may cause delays in the approval or the decision not to approve an application. Communications with the regulatory agencies during the approval process are also unpredictable; favorable communications early in the process do not ensure that approval will be obtained and unfavorable communications early on do not guarantee that approval will be denied. If we are unable to obtain approval for our product candidates in multiple jurisdictions, our revenue and results of operations could be negatively affected. Applications for our product candidates could fail to receive regulatory approval, or could be delayed in receiving regulatory approval, for many reasons, including but not limited to the following:

- regulatory authorities may disagree with the design, implementation, or conduct of our clinical studies;
- regulatory authorities may change their guidance or requirements for a development program for a product candidate;
- the population studied in the clinical program may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- regulatory authorities may disagree with our interpretation of data from nonclinical studies or clinical studies;
- the data collected from clinical studies of our product candidates may not be sufficient to support the submission of an NDA, or biologics license application, or BLA, or other submission or to obtain regulatory approval;
- we may be unable to demonstrate to regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities used to manufacture our clinical and commercial supplies;
- the U.S. government may be shut down, which could delay the FDA;
- failure of our nonclinical or clinical development to comply with an agreed upon Pediatric Investigational Plan (PIP), which details the designs and completion timelines for nonclinical and clinical studies and is a condition of marketing authorization in the EU; and
- the approval policies or regulations of regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Furthermore, the disease states we are evaluating often will not have clear regulatory paths for approval and/or do not have validated outcome measures. In these circumstances, we work closely with the regulatory authorities to define the approval path and may have to qualify outcome measures as part of our development programs. Additionally, many of the disease states we are targeting, such as LC-FAOD, are highly heterogeneous in nature, which may impact our ability to determine the treatment benefit of our potential therapies.

This lengthy and uncertain approval process, as well as the unpredictability of the clinical and nonclinical studies, may result in our failure to obtain regulatory approval to market any of our product candidates, or delayed regulatory approval, which would significantly harm our business, results of operations, and prospects.

The regulatory approval process for novel product candidates, such as our gene therapy product candidates, can be more expensive and take longer than for other product candidates, and may change in the future.

The clinical trial requirements of regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the product candidate. As a result, the regulatory approval process for novel product candidates such as our gene therapy product candidates can be more expensive and take longer than for other, better known or more extensively studied product candidates, which can lead to fewer product approvals. To date, very few gene therapy products have received regulatory approval in the United States or Europe.

Additionally, the FDA, Health Canada, and the EMA have each expressed interest in further regulating biotechnology, including gene therapy and genetic testing. For example, the EMA, which governs the development of gene therapies in the EU and may issue new guidelines concerning the development and marketing authorization for gene therapy products, advocates a risk-based approach to the development of a gene therapy product. Agencies at both the federal and state level in the United States, as well as U.S. congressional committees and foreign governments, have also expressed interest in further regulating the biotechnology industry. Different regulatory approaches by jurisdiction can result in different or additional preclinical studies or clinical trials being required to support regulatory approval in each jurisdiction.

Regulatory requirements such as review committees and advisory groups, the new guidelines they promulgate, and new guidance issued by regulatory authorities may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post- approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our or our collaborators' ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay, or halt clinical studies or further development, and could result in a more restrictive label, the delay or denial of regulatory approval by the FDA or other comparable foreign authorities, or a Risk Evaluation and Mitigation Strategy, or REMS, plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, restricted distribution, a communication plan for healthcare providers, and/or other elements to assure safe use. Our product candidates are in development and the safety profile has not been established. Further, as one of the goals of Phase 1 and/or 2 clinical trials is to identify the highest dose of treatment that can be safely provided to study participants, adverse side effects, including serious adverse effects, have occurred in certain studies as a result of changes to the dosing regimen during such studies. Gene therapy product candidates using AAV vectors, like DTX301, have been associated with immunologic reaction to the capsid protein or gene at early time points after administration. For example, in our discontinued Phase 1/2 clinical trial of DTX101 in hemophilia B, we observed elevated laboratory alanine transaminase levels, or ALTs. In previous clinical trials involving AAV viral vectors for gene therapy, some subjects experienced adverse events, including the development of a T-cell mediated immune response against the vector capsid proteins. In addition, theoretical side effects of AAV vectors include replication and spread of the virus to other parts of the body and insertional oncogenesis, which is the process whereby the insertion of a gene near a gene that is important in cell growth or division results in uncontrolled cell division, which could potentially enhance the risk of malignant transformation or cancer. Potential procedure-related events are similar to those associated with standard coronary diagnostic procedures, and may include vascular injury (e.g., damage to the femoral, radial or brachial arteries at the site of vascular access, or damage to the coronary arteries) or myocardial injury. Future product candidates may also cause these or similar side effects as development proceeds. Results of our studies or investigator-sponsored trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our studies could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny or withdraw approval of our product candidates for any or all targeted indications.

Drug-related side effects could affect patient recruitment and the ability of enrolled patients to complete a study. Such side effects could also result in potential product liability claims. We currently carry product liability insurance in the amount of $10.0 million per incident and $10.0 million in the aggregate, and we are required to maintain product liability insurance pursuant to certain of our agreements. We believe our product liability insurance coverage is sufficient in light of our current clinical programs; however, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability, or losses may exceed the amount of insurance that we carry. A product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. In addition, regardless of merit or eventual outcome, product liability claims may result in impairment of our business reputation, withdrawal of clinical study participants, costs due to related litigation, distraction of management's attention from our primary business, initiation of investigations by regulators, substantial monetary awards to patients or other claimants, the inability to commercialize our product candidates, and decreased demand for our product candidates, if approved for commercial sale.

Additionally, even though we received regulatory approval for Crysvita, Mepsevii, and Dojolvi and even if our product candidates receive marketing approval in the future, if we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the product's label or restrict the product's approved use;
- we may be required to create a REMS plan;
- patients and physicians may elect not to use our products, or reimbursement authorities may elect not to reimburse for them; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations, and prospects.

Serious adverse events in clinical trials involving gene therapy product candidates may damage public perception of the safety of our product candidates, increase government regulation, and adversely affect our ability to obtain regulatory approvals for our product candidates or conduct our business.

Gene therapy remains a novel technology. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. For example, certain gene therapy trials using AAV8 vectors (although at significantly higher doses than those used in our gene therapy product candidates) and other vectors led to several well-publicized adverse events, including cases of leukemia and death. The risk of cancer or death remains a concern for gene therapy and we cannot assure you that it will not occur in any of our planned or future clinical studies. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products, particularly AAV gene therapy products such as candidates based on the same capsid serotypes as our product candidates, or occurring during use of our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity, could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our gene therapy product candidates, stricter labeling requirements for those gene therapy product candidates that are approved and a decrease in demand for any such gene therapy product candidates, all of which would have an adverse effect on our business, financial condition, results of operations and prospects.

Even if we obtain regulatory approval for our product candidates, our products will remain subject to regulatory scrutiny.

Our products and any product candidates that are approved are subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, distribution, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA, and comparable foreign regulatory authority, requirements, including ensuring that quality control and manufacturing procedures conform to Good Manufacturing Practices (GMP) regulations. As such, we and our contract manufacturers will be subject to continual review and inspection to assess compliance with GMP and adherence to commitments made in any NDA, BLA, MAA, or other comparable application for approval in another jurisdiction. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or other conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical studies, and surveillance to monitor the safety and efficacy of the product candidate. We could also be asked to conduct post-marketing clinical studies to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval was obtained via the accelerated approval or conditional marketing authorization pathways, we would be required to conduct a successful post-marketing clinical study to confirm clinical benefit for our products. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval. We will be required to report certain adverse events and manufacturing problems, if any, to the FDA and comparable foreign regulatory authorities. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may promote our products only for indications or uses for which they have approval. The holder of an approved NDA, BLA, MAA, or other comparable application must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process.

If we fail to comply with applicable regulatory requirements, or there are safety or efficacy problems with a product, a regulatory agency or enforcement authority may, among other things:

- issue warning or notice of violation letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any of our ongoing clinical studies;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities;
- seize or detain products, or require a product recall; or
- require entry into a consent decree.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

If we are unable to identify, source, and develop effective biomarkers, or our collaborators are unable to successfully develop and commercialize companion diagnostics for our product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates.

We are developing companion diagnostic tests to identify the right patients for certain of our product candidates and to monitor response to treatment. In certain cases, diagnostic tests may need to be developed as companion diagnostics and regulatory approval obtained in order to commercialize some product candidates. We currently use and expect to continue to use biomarkers to identify the right patients for certain of our product candidates. We may also need to develop predictive biomarkers in the future. For example, to evaluate therapeutic response of DTX301, we are measuring ammonia levels and other biomarkers, including ^{13}C-acetate, which are established measures of OTC deficiency disease status and ureagenesis. We offer no assurances that ^{13}C-acetate or any other future potential biomarker will in fact prove predictive, be reliably measured, or be accepted as a measure of efficacy by the FDA or other regulatory authorities. In addition, our success may depend, in part, on the development and commercialization of companion diagnostics. We also expect the FDA will require the development and regulatory approval of a companion diagnostic assay as a condition to approval of our gene therapy product candidates. There has been limited success to date industrywide in developing and commercializing these types of companion diagnostics. Development and manufacturing of companion diagnostics is complex and there are limited manufacturers with the necessary expertise and capability. Even if we are able to find a qualified collaborator, it may not be able to manufacture the companion diagnostics at a cost or in quantities or on timelines necessary for use with our product candidates. To be successful, we need to address a number of scientific, technical and logistical challenges. We have not yet initiated development and commercialization of companion diagnostics. We have little experience in the development and commercialization of diagnostics and may not be successful in developing and commercializing appropriate diagnostics to pair with any of our product candidates that receive marketing approval. University of Pennsylvania School of Medicine currently conducts some of our clinical assays pursuant to a sponsored research agreement, one of which is required for our ongoing Phase 1/2 clinical trial. We also use third parties for the automation, characterization and validation, of our bioanalytical assays, companion diagnostics and the manufacture of its critical reagents.

Companion diagnostics are subject to regulation by FDA and similar regulatory authorities outside the United States as medical devices and require regulatory clearance or approval prior to commercialization. In the United States, companion diagnostics are

cleared or approved through FDA's 510(k) premarket notification or premarket approval, or PMA, process. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted 510(k) premarket notification, PMA or equivalent application types in jurisdictions outside the United States, may cause delays in the approval, clearance or rejection of an application. Given our limited experience in developing and commercializing diagnostics, we expect to rely in part or in whole on third parties for companion diagnostic design and commercialization. We and our collaborators may encounter difficulties in developing and obtaining approval or clearance for the companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by us or our collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of our product candidates.

Risks Related to our Reliance on Third Parties

We rely on third parties to conduct our nonclinical and clinical studies and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with regulatory requirements, we may be exposed to sub-optimal quality and reputational harm, we may not be able to obtain regulatory approval for or commercialize our product candidates, and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third parties, including CROs, collaborative partners, and independent investigators to analyze, collect, monitor, and manage data for our ongoing nonclinical and clinical programs. We rely on third parties for execution of our nonclinical and clinical studies, and for estimates regarding costs and efforts completed, and we control only certain aspects of their activities. For example, pursuant to the terms of our collaboration with GeneTx on the development of GeneTx's GTX-102, an antisense oligonucleotide (ASO) for the treatment of Angelman syndrome, subject to certain limited rights we have, GeneTx retains the decision-making authority on all matters in connection with the research, development, manufacturing and regulatory activities with respect to the program. With respect to our collaboration with Arcturus, we rely on our partner Arcturus for the design and optimization of initial product candidates under our mRNA, DNA and siRNA collaborations. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs and other vendors and partners are required to comply with GMP, GCP, and GLP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, and comparable foreign regulatory authorities for all of our product candidates in development. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, study sites, and other contractors. If we or any of our CROs or other vendors and partners, including the sites at which clinical studies are conducted, fail to comply with applicable regulations, the data generated in our nonclinical and clinical studies may be deemed unreliable and the FDA, EMA, or comparable foreign regulatory authorities may deny approval and/or require us to perform additional nonclinical and clinical studies before approving our marketing applications, which would delay the approval process. We cannot make assurances that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical studies comply with GCP regulations or that nonclinical studies comply with GLP regulations. In addition, our clinical studies must be conducted with products produced under GMP regulations. If the regulatory authorities determine that we have failed to comply with GLP, GMP, or GCP regulations, they may deny approval of our product candidates and/or we may be required to repeat clinical or nonclinical studies, which would delay the regulatory approval process.

Our CROs and other vendors and partners are not our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our on-going nonclinical and clinical programs. If our vendors and partners do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements, or for other reasons, our clinical studies may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. CROs and other vendors and partners may also generate higher costs than anticipated as a result of changes in scope of work or otherwise. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative vendors or do so on commercially reasonable terms. Switching or adding additional vendors involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new vendor commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our vendors and partners, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and business prospects.

We also rely on third parties in other ways, including efforts to support patient diagnosis and identify patients, to assist our finance and legal departments, and to provide other resources for our business. Use of these third parties could expose us to sub-optimal quality, missed deadlines, and non-compliance with applicable laws, all of which could result in reputational harm to us and negatively affect our business.

We are dependent on KKC for the clinical and commercial supply of Crysvita for all major markets and for the development and commercialization of Crysvita in certain major markets, and KKC's failure to provide an adequate supply of Crysvita or to commercialize Crysvita in those markets could result in a material adverse effect on our business and operating results.

Under our agreement with KKC, KKC has the sole right to commercialize Crysvita in Europe and, at a specified time, in the United States, Canada, and Turkey, subject to a limited promotion right we retained. Our partnership with KKC may not be successful, and we may not realize the expected benefits from such partnership, due to a number of important factors, including but not limited to the following:

- KKC has no obligation under our agreement to use diligent efforts to commercialize Crysvita in Europe. The timing and amount of any royalty payments that are made by KKC based on sales of Crysvita in Europe will depend on, among other things, the efforts, allocation of resources, and successful commercialization of Crysvita by KKC in Europe.
- the timing and amount of any payments we may receive under our agreement with KKC will depend on, among other things, the efforts, allocation of resources, and successful commercialization of Crysvita by KKC in the United States and Canada under our agreement;
- KKC may change the focus of its commercialization efforts or pursue higher-priority programs;
- KKC may make decisions regarding the indications for our product candidates in countries where it has the sole right to commercialize the product candidates that limit commercialization efforts in those countries or in countries where we have the right to commercialize our product candidates;
- KKC may make decisions regarding market access and pricing in countries where it has the sole right to commercialize our product candidates which can negatively impact our commercialization efforts in countries where we have the right to commercialize our product candidates;
- KKC may fail to manufacture or supply sufficient drug product of Crysvita in compliance with applicable laws and regulations or otherwise for our development and clinical use (including as a result of the COVID-19 pandemic), which could result in program delays;
- KKC may fail to manufacture or supply sufficient drug product of Crysvita in compliance with applicable laws and regulations or otherwise for our commercial use (including as a result of the COVID-19 pandemic), which could result in lost revenue;
- KKC may elect to develop and commercialize Crysvita indications with a larger market than XLH and at a lower price, thereby reducing the profit margin on sales of Crysvita for any orphan indications, including XLH;
- if KKC were to breach or terminate the agreement with us, we would no longer have any rights to develop or commercialize Crysvita or such rights would be limited to non-terminated countries;
- KKC may terminate its agreement with us, adversely affecting our potential revenue from licensed products; and
- the timing and amounts of expense reimbursement that we may receive are uncertain, and the total expenses for which we are obligated to reimburse KKC may be greater than anticipated.

We rely on third parties to manufacture our products and most of our product candidates and to acquire the raw material components to manufacture such products and product candidates. Our business could be harmed if those third parties fail to provide us with sufficient quantities of drug product, or fail to do so at acceptable quality levels or cost.

We have limited infrastructure or capability internally to manufacture our products and product candidates, and we currently lack the resources and the capability to manufacture our products and most of our product candidates on a clinical or commercial scale. We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our products and product candidates for our clinical studies. There are a limited number of suppliers for raw materials that we use to manufacture our drugs, placebos, or active controls, and there may be a need to identify alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our products and our product candidates for our clinical studies, and, if approved, ultimately for commercial sale. We also do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. We may also experience interruptions in supply of product if the product or raw material components fail to meet our quality control standards or the quality control standards of our suppliers. Any significant interruption in the supply of products due to delays in obtaining the raw material components or for other reasons could hinder our ability to distribute products to meet commercial demand and negatively impact our business. Any significant delay or discontinuity in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical study due to, among other things, the failure of a manufacturer to provide a drug substance or drug product of sufficient quantity or quality, or the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing, and potential regulatory approval of our product candidates, and could also impair named patient sale supply of our product candidates, which could harm our business and results of operations.

We have no experience as a company developing a manufacturing facility and may experience unexpected costs or delays or ultimately be unsuccessful in developing a facility .

We expect our future manufacturing strategy to involve the use of one or more CMOs as well as our own capabilities and infrastructure, including at our Woburn, MA facility or new facilities we may develop. We expect that development of our own process development facility will provide us with enhanced control of material supply for both clinical trials and the commercial market, enable the more rapid implementation of process changes, and allow for better long-term margins. However, we have no experience as a company in developing a manufacturing facility and may experience unexpected costs or delays or ultimately be unsuccessful in developing our own manufacturing facility or capability. Additionally, given that cGMP gene therapy manufacturing is a nascent industry, there are a small number of CMOs with the experience necessary to manufacture our gene therapy product candidates and we may have difficulty finding or maintaining relationships with such CMOs or hiring experts for internal manufacturing and accordingly, our production capacity may be limited. We may establish multiple manufacturing facilities as we expand our commercial footprint to multiple geographies, which may lead to regulatory delays or prove costly. Even if we are successful, our manufacturing capabilities could be affected by cost-overruns, unexpected delays, equipment failures, lack of capacity, labor shortages, natural disasters, power failures, program failures, and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business.

Gene therapy and mRNA, DNA and siRNA product candidates are novel, complex, expensive and difficult to manufacture. We could experience manufacturing problems that result in delays in developing and commercializing these programs or otherwise harm our business.

The manufacturing process used to produce our gene therapy, mRNA, DNA and siRNA product candidates is novel, complex, and has not been validated for commercial use. Several factors could cause production interruptions, including equipment malfunctions, regulatory inspections, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error or disruptions in the operations of our suppliers.

Our gene therapy, mRNA, DNA and siRNA product candidates require processing steps that are more complex than those required for most small molecule drugs. Moreover, unlike small molecules, the physical and chemical properties of a biologic such as gene therapy, mRNA, DNA and siRNA product candidates generally cannot be fully characterized. As a result, assays of the finished product candidate may not be sufficient to ensure that the product candidate is consistent from lot to lot or will perform in the intended manner. Accordingly, we employ multiple steps to control the manufacturing process to assure that the process works reproducibly, and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, noncompliance with regulatory requirements, product recalls, product liability claims or insufficient inventory. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, the EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, FDA, the EMA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, FDA, the EMA or other foreign regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects.

We also may encounter problems hiring and retaining the experienced scientific, quality-control and manufacturing personnel needed to operate the manufacturing processes for our gene therapy, mRNA, DNA and siRNA product candidates, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements. We may be unable to scale up existing or new facilities, including our facility in Woburn, MA, and such facilities may not enable the expansion of our internal manufacturing process discovery and development to the extent we anticipate, or at all.

We are subject to a multitude of manufacturing risks, any of which could substantially increase our costs and limit the supply of our product candidates.

The process of manufacturing our products and product candidates is complex, highly regulated, and subject to several risks, including but not limited to those listed below.

- The process of manufacturing our products and product candidates is extremely susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, or vendor or operator error. Even minor deviations from normal manufacturing processes for our products and any of our product candidates could result in reduced production yields, product defects, and other supply disruptions. If microbial, viral, or other contaminations are discovered in our products and product candidates or in the manufacturing facilities in which our products and product candidates are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination.
- The manufacturing facilities in which our products and product candidates are made could be adversely affected by equipment failures, labor shortages, raw material shortages, natural disasters, power failures, and numerous other factors.

Any adverse developments affecting manufacturing operations for our products and product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls, or other interruptions in the supply of our products and product candidates. For instance, during the fourth quarter of 2019, we experienced disruptions from our third-party supplier related to the fill and finish activities for the manufacture of Mepsevii, which negatively impacted our inventory of the product. Due to their stage of development, small volume requirements, and infrequency of batch production runs, we carry limited amounts of safety stock for our products and product candidates. We may also have to take inventory write-offs and incur other charges and expenses for products and product candidates that fail to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives.

The drug substance and drug product for our products and most of our product candidates are currently acquired from single-source suppliers. The loss of these suppliers, or their failure to supply us with the necessary drug substance or drug product, could materially and adversely affect our business.

We acquire most of the drug substances and drug products for our products and product candidates from single sources. If any single source supplier breaches an agreement with us, or terminates the agreement in response to an alleged breach by us or otherwise becomes unable to fulfill its supply obligations, we would not be able to manufacture and distribute the product or product candidate until a qualified alternative supplier is identified, which could significantly impair our ability to commercialize such product or delay the development of such product candidate. The drug substance and drug product for Crysvita are made by KKC pursuant to our license and collaboration agreement with KKC. The drug substance and drug product for Mepsevii are manufactured by Rentschler under a commercial supply and services agreement, accompanying purchase orders, and other agreements. The pharmaceutical-grade drug substance for Dojolvi is manufactured by IOI Oleo pursuant to our supply agreement with IOI Oleo, and the drug product for Dojolvi is prepared by Haupt Pharma AG and CPM pursuant to purchase orders. Single source suppliers are also used for our gene therapy programs. We have not currently secured any other suppliers for the drug substance or drug product of our products and product candidates and, although we believe that there are alternate sources of supply that could satisfy our clinical and commercial requirements, we cannot provide assurance that identifying alternate sources and establishing relationships with such sources would not result in significant expense or delay in the commercialization of our products or the development of our product candidates. For instance, we experienced disruptions from our third-party supplier related to the fill and finish activities for the manufacture of Mepsevii during the fourth quarter of 2019 and as a result, we have identified an alternative supplier to conduct such activities. It may take a significant amount of time and expense to qualify such alternative supplier and to transfer activities to such supplier, which are currently ongoing. If we fail to qualify our alternative supplier in a timely manner, we could experience delays or disruptions in the supply of Mepsevii, which would negatively impact sales of the product. Additionally, we may not be able to enter into supply arrangements with our alternative supplier on commercially reasonable terms or at all. The terms of any new agreement, such as any agreement with our alternative supplier for Mepsevii, may also be less favorable or more costly than the terms we have with our current supplier. A delay in the commercialization of our products or the development of our product candidates or having to enter into a new agreement with a different third-party on less favorable terms than we have with our current suppliers could have a material adverse impact upon on our business.

We and our collaborators and contract manufacturers are subject to significant regulation with respect to manufacturing our products and our product candidates. The manufacturing facilities on which we rely may not continue to meet regulatory requirements or may not be able to meet supply demands.

All entities involved in the preparation of therapeutics for clinical studies or commercial sale, including our existing contract manufacturers and collaboration partners for our product and product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical studies must be manufactured in accordance with GMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our products and product candidates that may not be detectable in final product testing. We, our collaborators, or our contract manufacturers must supply all necessary documentation in support of an NDA, BLA, MAA, or other application for regulatory approval, on a timely basis and must adhere to GLP, GMP, and similar regulations enforced by the FDA and other regulatory agencies through their facilities inspection programs. Some of our contract manufacturers have never produced a commercially approved pharmaceutical product and therefore have not obtained the requisite regulatory authority approvals to do so. The facilities and quality systems of some or all of our collaborators and third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our products, product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are substantially dependent on, our contract manufacturing partners for compliance with the regulatory requirements. If these facilities cannot schedule manufacturing to meet inspectional demands or do not initially pass and continue to pass regulatory inspections, including pre-approval plant inspections, regulatory approval of our product candidates may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever.

The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our collaborators, such as KKC, and third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third-party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales, recalls or seizures of product or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us, our collaborators, or third parties with whom we contract could materially harm our business.

If we, our collaborators, including KKC, or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA or other applicable regulatory authority can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, withdrawal of an approval, or suspension of production. As a result, our business, financial condition, and results of operations may be materially harmed.

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified through an NDA or BLA supplement or MAA variation, or equivalent foreign regulatory filing, which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause us to incur higher costs and could cause interruptions in the supply of our products or a delay or termination of clinical studies, regulatory submissions, required approvals, or commercialization of our product candidates. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, we could experience supply interruptions of product that would impact our ability to meet commercial demand and result in loss of revenue, or our clinical studies may be delayed, which could delay regulatory approval for our product candidates, any and all of which could materially and adversely affect our business.

The actions of distributors and specialty pharmacies could affect our ability to sell or market products profitably. Fluctuations in buying or distribution patterns by such distributors and specialty pharmacies could adversely affect our revenues, financial condition, or results of operations.

We rely on commercial distributors and specialty pharmacies for a considerable portion of our product sales and such sales are concentrated within a small number of distributors and specialty pharmacies. The financial failure of any of these parties could adversely affect our revenues, financial condition or results of operations. Our revenues, financial condition or results of operations may also be affected by fluctuations in buying or distribution patterns of such distributors and specialty pharmacies. These fluctuations may result from seasonality, pricing, wholesaler inventory objectives, or other factors.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties in connection with the development and manufacture of our products and product candidates and will likely rely on third parties in connection with the commercialization of our approved products, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements, letters of engagement, or other similar agreements with our collaborators, advisors, employees, and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

Risks Related to Commercialization of Our Products and Product Candidates

If the market opportunities for our products and product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. Because the target patient populations of our products and product candidates are small, and the addressable patient population potentially even smaller, we must be able to successfully identify patients and acquire a significant market share to achieve profitability and growth.

We focus our research and product development on treatments for rare and ultra-rare genetic diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare and ultra-rare genetic diseases. Some of our current clinical programs may be most appropriate for patients with more severe forms of their disease. For instance, our Phase 2 study of Dojolvi in LC-FAOD enrolled patients with more severe disease. In addition, while adults make up the majority of the XLH patients, they often have less severe disease that may reduce the penetration of Crysvita in the adult population relative to the pediatric population. Given the overall rarity of the diseases we target, it is difficult to project the prevalence of the more severe forms, or the other subsets of patients that may be most suitable to address with our products and product candidates, which may further limit the addressable patient population to a small subset. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our products and product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our products and product candidates may be limited or may not be amenable to treatment with our products and product candidates, and new patients may become increasingly difficult to identify or access, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our products and product candidates, because the potential target populations are very small, we may never become or remain profitable nor generate sufficient revenue growth to sustain our business.

Manufacturers that produce our products and product candidates may not have experience producing our products and product candidates at commercial levels and may not achieve the necessary regulatory approvals or produce our products and product candidates at the cost, quality, quantities, locations, and timing needed to support profitable commercialization.

We rely on third-party manufacturers to produce our products and product candidates. These manufacturers may not have the experience or ability to produce our products and product candidates at commercial levels. We may run into technical or scientific issues related to manufacturing or development that we may be unable to resolve in a timely manner or with available funds. We also have not completed all of the characterization and validation activities necessary for commercialization and regulatory approvals for all of our product candidates. If our manufacturing partners are not able to conduct all such necessary activities in accordance with applicable regulations, our commercialization efforts will be harmed. We have not yet secured manufacturing capabilities for commercial quantities of all of our product candidates and may be unable to negotiate binding agreements with manufacturers to support our commercialization activities on commercially reasonable terms.

Even if our third-party product manufacturers develop an acceptable manufacturing process, if such third-party manufacturers are unable to produce the necessary quantities of our products and product candidates, are unable to comply with GMP or other pertinent regulatory requirements, or are unable to produce our products and product candidates within our planned timeframe and cost parameters, the development and sales of our products and product candidates, if approved, may be materially harmed.

Additionally, the cost to us for the supply of our products and product candidates manufactured by such third parties may be high and could limit our profitability, even if our third-party product manufacturers develop acceptable manufacturing processes that provide the necessary quantities of our products and product candidates in a compliant and timely manner. Furthermore, KKC is our sole supplier of commercial quantities of Crysvita. The supply price to us for commercial sales of Crysvita in Latin America and the transfer price for commercial sales of the product in the United States and Canada is 35% of net sales through December 31, 2022 and 30% thereafter, which is higher than the typical cost of goods sold by companies focused on rare diseases.

We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that are similar, more advanced, or more effective than ours, which may adversely affect our financial condition and our ability to successfully commercialize our product candidates.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We are currently aware of various existing treatments that may compete with our products and product candidates. For example, XLH is treated with oral phosphate and vitamin D therapy, which may compete with Crysvita; LC-FAOD is managed with diet therapy and medium-chain triglyceride oil, which may compete with Dojolvi; OTC deficiency is currently treated with nitrogen scavenging drugs and severe limitations in dietary protein, which may compete with DTX30; and GSDIa is currently treated with corn starch, which may compete with DTX401. Triheptanoin is available in food-grade form, which may compete with our pharmaceutical-grade product. Furthermore, investigator-sponsored trials evaluating triheptanoin in multiple indications are ongoing. Gene therapy, gene correction, RNA-based therapies, and other approaches may also emerge for the treatment of any of the disease areas in which we focus.

We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies, startups, academic research institutions, government agencies, and public and private research institutions. Many of our competitors have substantially greater financial, technical, and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and marketing their products as well. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring, or licensing on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop, or achieve earlier patent protection, regulatory approval, product commercialization, and market penetration than we do. Additionally, technologies developed by our competitors may render our potential products and product candidates uneconomical or obsolete, and we may not be successful in marketing our products and product candidates against competitors.

We continue to build and evolve an integrated commercial organization. If we are unable to expand our existing commercial infrastructure or enter into agreements with third parties to market and sell our products and product candidates, as needed, we may be unable to generate significant revenue.

In order to successfully commercialize our products as well as any additional products that may result from our development programs, we are building a commercial infrastructure in North America, Europe and Latin America. This infrastructure consists of both office based as well as field teams with technical expertise, and will be expanded as we approach the potential approval dates of additional products that result from our development programs. This will be expensive and time consuming. Any failure or delay in the expansion of this infrastructure may adversely impact the commercialization of our approved products.

Although our employees may have promoted other similar products in the past while employed at other companies, we, as a company, have limited, recent experience selling and marketing our product. Further, given our limited experience in marketing and selling biopharmaceutical products, our initial estimate of the size of the required field force may be materially more or less than the size of the field force actually required to effectively commercialize our product candidates. As such, we may be required to hire large teams to adequately support the commercialization of our products and product candidates or we may incur excess costs in an effort to optimize the hiring of commercial personnel. With respect to certain geographical markets, we may enter into collaborations with other entities to utilize their local marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If our future collaborators do not commit sufficient resources to commercialize our future products, if any, and we are unable to develop the necessary marketing capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We may be competing with companies that currently have extensive and well-funded marketing and sales operations. Without a large internal team or the support of a third-party to perform key commercial functions, we may be unable to compete successfully against these more established companies.

Our exclusive right to promote Crysvita in the United States and Canada expires in 2023.

Pursuant to the terms of our collaboration and license agreement with KKC, we have the sole right to promote Crysvita in the United States and Canada, or the profit-share territory, for a specified period of time, with KKC increasingly participating in the promotion of the product until the transition date of April 2023, which is the fifth anniversary of the commercial launch of the product in the United States. After the transition date, KKC will have the right to promote the product, subject to a limited promotion right retained by us. Although we expect that we will use our North America commercial infrastructure to promote our other commercialized products after the transition date, we cannot assure that we will have adequate commercial activity to support our field force and other aspects of our commercial infrastructure in the territory. After the transition date, we will also solely bear the expenses related to the promotion of Crysvita in the profit-share territory pursuant to our limited promotion right, rather than share such expenses with KKC. We expect to collaborate with KKC to provide for a seamless transition of responsibilities for KKC to promote the product in the profit-share territory after the transition date, however, the commercial success of Crysvita in the profit-share territory after the transition date will depend on, among other things, the efforts and allocation of resources of KKC.

The commercial success of any current or future product will depend upon the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community.

Even with the requisite approvals from the FDA and comparable foreign regulatory authorities, the commercial success of our current and future products will depend in part on the medical community, patients, and payors accepting our current and future products as medically useful, cost-effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients, payors, and others in the medical community. The degree of market acceptance of any of our current and future products will depend on a number of factors, including:

- the efficacy of the product as demonstrated in clinical studies and potential advantages over competing treatments;
- the prevalence and severity of any side effects, including any limitations or warnings contained in a product's approved labeling;
- the clinical indications for which approval is granted;
- relative convenience and ease of administration;
- the cost of treatment, particularly in relation to competing treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the effectiveness of our field forces and marketing efforts;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party insurance coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in nonclinical and clinical studies, market acceptance of the product will not be fully known until after it is launched. Our efforts to educate the medical community and payors on the benefits of the product candidates may require significant resources and may never be successful. If our current and future products fail to achieve an adequate level of acceptance by physicians, patients, payors, and others in the medical community, we will not be able to generate sufficient revenue to become or remain profitable.

The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.

Our target patient populations are small, and accordingly the pricing, coverage, and reimbursement of our products and product candidates, if approved, must be adequate to support our commercial infrastructure. Our per-patient prices must be sufficient to recover our development and manufacturing costs and potentially achieve profitability. We expect the cost of a single administration of gene therapy products, such as those we are developing, to be substantial, when and if they achieve regulatory approval. Accordingly, the availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to afford expensive treatments such as ours, assuming approval. Sales of our products and product candidates, if approved, will depend substantially, both domestically and abroad, on the extent to which their costs will be paid for by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other payors. If coverage and reimbursement are not available, are available only to limited levels, or are not available on a timely basis, we may not be able to successfully commercialize our products and product candidates, if approved. For example, deteriorating economic conditions and political instability in certain Latin American countries and in Turkey may cause us to experience significant delays in receiving approval for reimbursement for our products and consequently impact our product commercialization timelines in such regions. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to sustain our overall enterprise.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS or private payors will decide with respect to reimbursement for products such as ours, especially our gene therapy product candidates as there is a limited body of established practices and precedents for gene therapy products.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries will put pressure on the pricing and usage of our products and product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medicinal products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products and, as a result, they may not cover or provide adequate payment for our products and product candidates. We expect to experience pricing pressures in connection with the sale of any of our products and product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, additional legislative changes, and statements by elected officials. For example, proposals are being discussed to tie U.S. drug prices to the cost in other countries, several states in the U.S. have introduced legislation to require pharmaceutical companies to disclose their costs to justify the prices of their products, and an “Affordable Drug Pricing Task-Force” has been formed in the U.S. House of Representatives with the goal of combating the increased costs of prescription drugs. Although a number of these proposals and other measures, including the four executive orders announced by the U.S. Presidential administration in July 2020 aimed to lower drug prices, may require additional authorization to become effective, Congress and the U.S. Presidential administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. The downward pressure on healthcare costs in general, and with respect to prescription drugs, surgical procedures, and other treatments in particular, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

The results of the United Kingdom’s referendum on withdrawal from the EU may have a negative effect on our business, global economic conditions, and financial markets.

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit. On January 30, 2020, the United Kingdom formally withdrew from the EU. Following the United Kingdom’s formal withdrawal from the EU, the United Kingdom will to continue to follow all of the EU’s rules and its trading relationship with the EU will remain the same during a transition period which will expire on December 31, 2020. Several aspects of the United Kingdom and EU relationship will need to be determined during the transition period, including free trade agreements and rules and regulations affecting the biotechnology or pharmaceutical industries. Since a significant proportion of the regulatory framework in the United Kingdom is derived from EU directives and regulations, Brexit could materially impact the regulatory regime with respect to the approval of product candidates, disrupt the manufacture of our products and product candidates in the United Kingdom or the EU, disrupt the importation and export of active substances and other components of drug formulations, and disrupt the supply chain for clinical trial product and final authorized formulations. Any delay in obtaining, or an inability to obtain, any marketing approvals, or disruption to our and our collaborators’ supply chain as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the EU and restrict our ability to generate revenue and achieve and sustain profitability. The cumulative effect of disruptions to the regulatory framework or supply chains may add considerably to the development lead time to, and expense of, marketing authorization and commercialization of products in the EU and/or the United Kingdom. In view of the uncertainty surrounding the Brexit implementation, we are unable to predict the effects of such disruption to the regulatory framework and supply chain in Europe.

Further, these developments, or the perception that any of them could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Asset valuations, currency exchange rates and credit ratings may be especially subject to increased market volatility. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which EU laws to replace or replicate following the expiration of the transition period, including financial laws and regulations, tax and free trade agreements, intellectual property rights, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws, could decrease foreign direct investment in the United Kingdom, increase costs and depress economic activity. In addition, we expect that Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the United Kingdom determines which EU laws to replicate or replace. We are taking certain precautionary measures with respect to Brexit and its impact to the EU, and will continue to monitor the situation. If the United Kingdom were to significantly alter its regulations affecting the biotechnology or pharmaceutical industries, we could face significant new costs. It may also be time-consuming and expensive for us to alter our internal operations in order to comply with new regulations. Any of these factors could have a material adverse effect on our business, financial condition and results of operations and affect our strategy in the U.K. and EU biotech market.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain effective patent rights for our products, product candidates, or any future product candidates, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection, and confidentiality agreements to protect the intellectual property related to our technologies, our products, and our product candidates. Our success depends in large part on our and our licensors' ability to obtain and maintain patent and other intellectual property protection in the United States and in other countries with respect to our proprietary technology, our products, and our product candidates.

We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and products that are important to our business. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal and factual questions for which legal principles remain unsolved. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our products or product candidates in the United States or in other foreign countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue, and even if such patents cover our products or product candidates, third parties may challenge their validity, enforceability, or scope, which may result in such patents being narrowed, found unenforceable, or invalidated. Furthermore, even if the patents and patent applications we own or in-license are unchallenged, they may not adequately protect our intellectual property, provide exclusivity for our products or product candidates, or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

We, independently or together with our licensors, have filed several patent applications covering various aspects of our products or product candidates. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

Although we have a number of patents or applications covering methods of use and certain compositions of matter, we do not have complete patent protection for our products and product candidates in all territories. For example, there are no issued patents covering the Crysvita composition of matter in Latin America where we have rights to commercialize the compound. Therefore, a competitor could develop the same antibody or a similar antibody as well as other approaches that target FGF23 for potential commercialization in Latin America, subject to any intellectual property rights or regulatory exclusivities awarded to us. If we cannot obtain and maintain effective patent rights for our products or product candidates, we may not be able to compete effectively and our business and results of operations would be harmed.

We may not have sufficient patent terms to effectively protect our products and business.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its effective filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications.

While patent term extensions under the Hatch-Waxman Act in the United States and under supplementary protection certificates in Europe may be available to extend the patent exclusivity term for Crysvita, Mepsevii, Dojolvi, DTX301, and DTX401, we cannot provide any assurances that any such patent term extension will be obtained and, if so, for how long. Furthermore, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we do not have sufficient patent terms or regulatory exclusivity to protect our products, our business and results of operations may be adversely affected.

Patent policy and rule changes could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. We therefore cannot be certain that we or our licensors were the first to make the invention claimed in our owned and licensed patents or pending applications, or that we or our licensor were the first to file for patent protection of such inventions. Assuming the other requirements for patentability are met, in the United States prior to March 16, 2013, the first to make the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. After March 15, 2013, under the Leahy-Smith America Invents Act, or the Leahy-Smith Act, enacted on September 16, 2011, the United States has also moved to a first to file system. The Leahy-Smith Act included a number of significant changes that affect the way patent applications are prosecuted and the way patents can be challenged. The effects of these changes are currently unclear as the courts have only begun to address these provisions. In general, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

If we are unable to maintain effective proprietary rights for our products, product candidates, or any future product candidates, we may not be able to compete effectively in our markets.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our products or product candidate discovery and development processes that involve proprietary know-how, information, or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors, and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, advisors, and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret.

Claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of others. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, *inter partes* reviews, post grant reviews, oppositions, and reexamination proceedings before the USPTO and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by other parties, exist in the fields in which we are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our products or product candidates may be subject to claims of infringement of the patent rights of these other parties.

Other parties may assert that we are employing their proprietary technology without authorization. There may be patents or patent applications with claims to materials, formulations, methods of manufacture, or methods for treatment related to the use or manufacture of our products or product candidates. We have conducted freedom to operate analyses with respect only to our products and certain of our product candidates, and therefore we do not know whether there are any patents of other parties that would impair our ability to commercialize all of our product candidates. We also cannot guarantee that any of our analyses are complete and thorough, nor can we be sure that we have identified each and every patent and pending application in the United States and abroad that is relevant or necessary to the commercialization of our products or product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our products or product candidates may infringe.

We are aware of four third-party patent families that include issued U.S. patents with claims that, if valid and enforceable, could be construed to cover one or more of our gene therapy product candidates, if and when approved, or methods of their manufacture. We are also aware of two third-party patent families that include issued European claims that, if valid and enforceable, could be construed to cover certain methods that may be used in the manufacture of one or more of our gene therapy product candidates. In addition, other parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any of these patents were held by a court of competent jurisdiction to cover aspects of our formulations, the manufacturing process of our products or any of our product candidates, methods of use, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize our products or a product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to continue commercialization of our products, or block our ability to develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products, or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to the intellectual property, through licenses from third parties and under patents that we own, to commercialize our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license, or use these proprietary rights. For example, our product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer.

We may face competition from biosimilars, which may have a material adverse impact on the future commercial prospects of Crysvita, Mepsevii, DTX301, and DTX401.

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars with respect to Crysvita, Mepsevii, DTX301, and DTX401. In the United States, the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, was included in the Affordable Care Act and created an abbreviated approval pathway for biological products that are demonstrated to be "highly similar," or biosimilar, to or "interchangeable" with an FDA-approved biological product. The BPCI Act prohibits the FDA from approving a biosimilar or interchangeable product that references a brand biological product until 12 years after the licensure of the reference product, but permits submission of an application for a biosimilar or interchangeable product to the FDA four years after the reference product was first licensed. The BPCI Act does not prevent another company from developing a product that is highly similar to the innovative product, generating its own data, and seeking approval. Moreover, it is not known whether the BPCI Act will survive in whole or in part if the Affordable Care Act is repealed by Congress or held unconstitutional by courts. As a result, its ultimate impact, implementation, meaning, and long-term existence are subject to uncertainty. Elimination or modification of the BPCI Act, or changes to the FDA's interpretation or implementation of the BPCI Act, could have a material adverse effect on the future commercial prospects for Crysvita, Mepsevii, DTX301, and DTX401.

In Europe, the European Commission has granted marketing authorizations for several biosimilars pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data supporting approval of an innovative biological product, but will not be able to get on the market until 10 years after the time of approval of the innovative product. This 10-year marketing exclusivity period will be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilars in other countries that could compete with our products.

If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

Additional competitors could enter the market with generic versions of our small-molecule product candidates, which may result in a material decline in sales of Dojolvi or future small-molecule product candidates.

Under the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application, or ANDA, seeking approval of a generic copy of an approved innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit an NDA under section 505(b)(2) that references the FDA's finding of safety and effectiveness of a previously approved drug. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. Innovative small molecule drugs may be eligible for certain periods of regulatory exclusivity (*e.g.*, five years for new chemical entities, three years for changes to an approved drug requiring a new clinical study, and seven years for orphan drugs), which preclude FDA approval (or in some circumstances, FDA filing and review of) an ANDA or 505(b)(2) NDA relying on the FDA's finding of safety and effectiveness for the innovative drug. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the "Orange Book." If there are patents listed in the Orange Book, a generic applicant that seeks to market its product before expiration of the patents must include in the ANDA or 505(b)(2) what is known as a "Paragraph IV certification," challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to enforce its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, competitors could file ANDAs for generic versions of Dojolvi, or 505(b)(2) NDAs that reference Dojolvi. If there are patents listed for Dojolvi in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict whether any patents issuing from our pending patent applications will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any patents that are granted and listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could more immediately face generic competition and its sales would likely decline materially. Should sales decline, we may have to write off a portion or all of the intangible assets associated with the affected product and our results of operations and cash flows could be materially and adversely affected.

The patent protection and patent prosecution for some of our product candidates is dependent on third parties.

While we normally seek and gain the right to fully prosecute the patents relating to our product candidates, there may be times when patents relating to our product candidates are controlled by our licensors. This is the case with our agreement with KKC, who is primarily responsible for the prosecution of patents and patent applications licensed to us under the collaboration agreement.

In addition, we have in-licensed patents and patent applications owned by the University of Pennsylvania, relating to the AAV8 vector used in DTX301 and DTX401. These patents and patent applications are licensed or sublicensed by REGENXBIO and sublicensed to us. We do not have the right to control the prosecution of these patent applications, or the maintenance of any of these patents. In addition, under our agreement with REGENXBIO, we do not have the first right to enforce the licensed patents, and our enforcement rights are subject to certain limitations that may adversely impact our ability to use the licensed patents to exclude others from commercializing competitive products. Moreover, REGENXBIO and the University of Pennsylvania may have interests which differ from ours in determining whether and the manner in which to enforce such patents.

If KKC, the University of Pennsylvania, or any of our future licensing partners fail to appropriately prosecute, maintain, and enforce patent protection for the patents covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using, and selling competing products. In addition, even where we now have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to us assuming control over patent prosecution.

If we fail to comply with our obligations in the agreements under which we license intellectual property and other rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, we may be required to make certain payments to the licensor, we may lose the exclusivity of our license, or the licensor may have the right to terminate the license, in which event we would not be able to develop or market products covered by the license. Additionally, the milestone and other payments associated with these licenses will make it less profitable for us to develop our drug candidates.

In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues. Disputes may arise regarding intellectual property subject to a licensing agreement, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our collaborators; and
- the priority of invention of patented technology.

If disputes over intellectual property and other rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

Although we are not currently involved in any intellectual property litigation, we may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. Although we are not currently involved in any intellectual property litigation, if we or one of our licensing partners were to initiate legal proceedings against a third party to enforce a patent covering our products or one of our product candidates, the defendant could counterclaim that the patent covering our product or product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable.

Interference proceedings or derivation proceedings now available under the Leahy-Smith Act provoked by third parties or brought by us or declared or instituted by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. In addition, the validity of our patents could be challenged in the USPTO by one of the new post grant proceedings (*i.e.*, *inter partes* review or post grant review) now available under the Leahy-Smith Act. Our defense of litigation, interference proceedings, or post grant proceedings under the Leahy-Smith Act may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise sufficient capital to continue our clinical studies, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We employ certain individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and independent contractors do not use the proprietary information or know-how of others in their work for us, and we are not currently subject to any claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties, we may in the future be subject to such claims. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distract management and other employees.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

Although we are not currently experiencing any claims challenging the inventorship of our patents or ownership of our intellectual property, we may in the future be subject to claims that former employees, collaborators, or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail to successfully defend against such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distract management and other employees.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and pharmaceutical industries involves both technological and legal complexity. Therefore, obtaining and enforcing such patents is costly, time consuming, and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. For example, in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the Supreme Court ruled that a "naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated," invalidating Myriad Genetics' patents on the BRCA1 and BRCA2 genes. Certain claims of our licensed U.S. patents covering DTX301 and DTX401 relate to isolated AAV8 vectors, capsid proteins, or nucleic acids. To the extent that such claims are deemed to be directed to natural products, or to lack an inventive concept above and beyond an isolated natural product, a court may decide the claims are invalid under *Myriad*. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, and defending patents on our products or product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Further, licensing partners such as KKC may not prosecute patents in certain jurisdictions in which we may obtain commercial rights, thereby precluding the possibility of later obtaining patent protection in these countries. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Risks Related to Our Business Operations

Actual or threatened public health epidemics or outbreaks, including the current COVID-19 pandemic, could materially and adversely impact our business and operating results.

A public health epidemic or outbreak, and the public and governmental efforts to mitigate the spread of such disease, could materially and adversely impact the commercialization of our products, development and regulatory approval of our product candidates and our clinical trial operations and significantly disrupt our business operations as well as those of our third party suppliers, CRO and collaboration partners that we rely on. In December 2019, a new strain of novel coronavirus (COVID-19) emerged in Wuhan, Hubei Province, China. In March 2020, the World Health Organization declared COVID-19 a pandemic. The spread of this pandemic has caused significant volatility and uncertainty in U.S. and international markets and could materially and adversely affect our business and operating results.

The rapid global spread of COVID-19 has led to the implementation of various responses, including government-imposed quarantines, business closures and lockdowns, shelter-in-place and social distancing mandates, sweeping restrictions on travel and other public health safety measures, as well as reported adverse impacts on healthcare resources, facilities and providers across the United States and in other countries where we operate. Although COVID-19 has already impacted our operations and those of our third-party partners, the ultimate scope and magnitude of such impact will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the scope and duration of the outbreak, additional or modified government actions, new information which may emerge concerning the severity of the coronavirus and the actions taken to contain the pandemic or treat its impact, among others.

Our clinical trial activities, including the initiation and completion of such activities and the timing thereof, have been and are expected to continue to be significantly delayed or disrupted by COVID-19. For instance, enrollment of patients in certain of our clinical trials for our gene therapy product candidates have been disrupted and dosing in certain of our trials has been delayed as shelter-in-place orders or quarantines have impeded patient movement. We may also experience difficulties in recruiting clinical site investigators and clinical site staff. Changes in local regulations in response to COVID-19 have also required us to change the way our clinical trials are conducted and certain anticipated data from our clinical trials will be delayed as a result. Further, healthcare resources have been and may continue to be diverted away from the conduct of clinical trials, such as the diversion of hospitals serving as our clinical trial sites, in response to the COVID-19 pandemic. Any of these events, including if we are required to initiate new or additional sites in response to such events, could require us to incur substantial increased expenses, delay the development and commercialization of our product candidates, delay the timing of anticipated data releases, and impact our operating results.

The COVID-19 pandemic may also impact the timing of review of our submissions and discussions with regulatory agencies, such as the FDA, with respect to our product candidates. The pandemic has also significantly impacted our commercialization efforts for our products, including the launch of our recently approved product, Dojolvi. Social distancing measures and travel limitations have prevented our field sales and medical teams from meeting with health care professionals, customers and patients in person and it has become increasingly difficult to maintain consistent contact with our current patients or identify new patients for our commercialized products and product candidates. Further, certain of our patients may experience interruptions in insurance coverage due to job loss or change in employment status due to the economic impact from the pandemic. Effects from government budgetary

constraints, either in the United States or internationally, due to the economic impact of the pandemic, such as changes to state coverage rules under Medicaid programs in the United States, could also impact continued insurance coverage and reimbursement for our products. Any of these events could impact our ability to commercialize our products and adversely affect our operating results and revenue.

The continuing spread of the COVID-19 pandemic may also result in the inability of our suppliers to deliver drug product or raw materials on a timely basis, if at all, or result in increased costs or expenses. Facility shutdowns or operational restrictions imposed by government-imposed mandates could result in supply disruptions that could impact the availability of drug product for our clinical trials as well as our commercialized products. For instance, certain of our third party manufacturers or suppliers have prioritized and allocated more resources and capacity to supply drug product or raw materials to other companies engaged in the study of potential treatments or vaccinations for COVID-19, which may result in delays or shortages in supply of such product or materials to us. Any of these events could adversely impact our clinical trial activities and our ability to meet commercial demand for our product and product candidates and result in loss of revenue. In response to these events, we are currently seeking alternative sources of supply of drug product or raw materials in an attempt to avoid future potential delays in supply of product, which may result in additional expenses.

In an effort to protect the health of our employees, their families and our communities, and in accordance with shelter-in-place direction from state and local government authorities, we have restricted access to our facilities to personnel and third parties who must perform critical activities that must be completed on-site, limited the number of such personnel that can be present at our facilities at any one time, and requested that most of our personnel work remotely, including significant limitations on access to our laboratory space. The effects of the shelter-in-place and our remote working policies may negatively impact productivity and disrupt our business operations. Further, notwithstanding these measures, the COVID-19 pandemic could affect the health and availability of our workforce, including members of our management. If members of our management and other key personnel in critical functions across our organization are unable to perform their duties or have limited availability due to illness from COVID-19, we may not be able to execute on our business strategy and/or our operations may be negatively impacted. The magnitude of the adverse effect on our business operations will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course.

The COVID-19 pandemic has negatively impacted the global economy, disrupted global supply chains and created significant volatility and disruption of financial markets, which could adversely impact our operating results. For instance, delays or defaults in payments by our customer and third-party partners could adversely impact our accounts receivables. The value of our investments currently held in a variety of accounts could also be negatively impacted by the volatility in certain markets, such as the fixed income market, and impact our sources of liquidity. The stock market in general and the stock price of biopharmaceutical companies, in particular, have also experienced extreme price and volume fluctuations. Broad market and industry factors, including worsening economic conditions or a recession resulting from the ongoing COVID-19 pandemic, may adversely impact the value of our common stock and our ability to raise capital. If we do raise additional capital and issue equity securities when the value of our common stock is depressed, the dilutive impact on our stockholders may be greater compared to when the value of our common stock is higher.

The COVID-19 pandemic continues to rapidly evolve. The magnitude and extent to which the outbreak may impact our business operations, clinical trial activities, product candidate approvals, supply chain and commercialization of our products and product candidates will continue to remain highly dependent on future developments, which are very uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak and additional restrictions to contain the outbreak and the effectiveness of such actions taken in the United States and other countries to contain and address the pandemic. This pandemic may also amplify many of the other risks described throughout the “Risk Factors” section of this Quarterly Report on Form 10-Q.

Our future success depends in part on our ability to retain our Founder, President, and Chief Executive Officer and to attract, retain, and motivate other qualified personnel.

We are dependent on Emil D. Kakkis, M.D., Ph.D., our Founder, President, and Chief Executive Officer, the loss of whose services may adversely impact the achievement of our objectives. Dr. Kakkis could leave our employment at any time, as he is an “at will” employee. Recruiting and retaining other qualified employees, consultants, and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled personnel in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical studies may make it more challenging to recruit and retain qualified personnel. The inability to recruit and retain qualified personnel, or the loss of the services of Dr. Kakkis, may impede the progress of our research, development, and commercialization objectives.

If we fail to obtain or maintain orphan drug exclusivity for our products, our competitors may sell products to treat the same conditions and our revenue will be reduced.

Our business strategy focuses on the development of drugs that are eligible for FDA and EU orphan drug designation. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Because the extent and scope of patent protection for our products may in some cases be limited, orphan drug designation is especially important for our products for which orphan drug designation may be available. For eligible drugs, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug exclusivity for our drug products and biologic products that do not have broad patent protection, our competitors may then sell the same drug to treat the same condition sooner than if we had obtained orphan drug exclusivity, and our revenue will be reduced.

Even though we have orphan drug designation for Dojolvi for the treatment of fatty acid oxidation disorders in the United States and for various subtypes of LC-FAOD in Europe, as well as for Crysvita, Mepsevii, DTX301 and DTX401 in the United States and Europe, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition or the same drug can be approved for a different indication unless there are other exclusivities such as new chemical entity exclusivity preventing such approval. Even after an orphan drug is approved, the FDA or EMA can subsequently approve the same drug with the same active moiety for the same condition if the FDA or EMA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.

As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, field forces, marketing, financial, legal, and other resources. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees, and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenue could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

Our operating results would be adversely impacted if our intangible assets become impaired.

As a result of the accounting for our acquisition of Dimension Therapeutics, Inc. (Dimension) in November 2017, we have recorded on our balance sheet intangible assets for in-process research and development (IPR&D) related to DTX301 and DTX401. Following the FDA approval of Dojolvi, we have also recorded contract-based intangible assets related to our license from third parties for certain assets related to the product. We test the intangible assets for impairment annually during the fourth quarter and more frequently if events or changes in circumstances indicate that it is more likely than not that the asset is impaired. If the associated research and development effort is abandoned, the related assets will be written-off and we will record a noncash impairment loss on our statement of operations. We have not recorded any impairments related to our intangible assets through the end of June 30, 2020.

We may not be successful in our efforts to identify, license, discover, develop, or commercialize additional product candidates.

Although a substantial amount of our effort will focus on the continued clinical testing, potential approval, and commercialization of our existing product candidates, the success of our business also depends upon our ability to identify, license, discover, develop, or commercialize additional product candidates. Research programs to identify and develop new product candidates, such as those under our collaboration with Arcturus, require substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. Our research programs or licensing efforts may fail to yield additional product candidates for clinical development and commercialization for a number of reasons, including but not limited to the following:

- our research or business development methodology or search criteria and process may be unsuccessful in identifying potential product candidates;
- we may not be able or willing to assemble sufficient technical, financial or human resources to acquire or discover additional product candidates;
- we may face competition in obtaining and/or developing additional product candidates;
- our product candidates may not succeed in research, discovery, preclinical or clinical testing;
- our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may be covered by third parties' patents or other exclusive rights;
- the market for a product candidate may change during our program so that such a product may become unreasonable to continue to develop;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost or at all; and
- a product candidate may not be accepted as safe and effective by regulatory authorities, patients, the medical community, or payors.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, or we may not be able to identify, license, discover, develop, or commercialize additional product candidates, which would have a material adverse effect on our business and could potentially cause us to cease operations.

We may expend our limited resources to pursue a particular product, product candidate or indication and fail to capitalize on products, product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus our sales, marketing and research programs on certain products, product candidates or for specific indications. As a result, we may forego or delay pursuit of opportunities with other products or product candidates or other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product or product candidate, we may relinquish valuable rights through collaboration, licensing, or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

If we are unable to maintain effective internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our stock may decrease.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we are required to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404(a) of the Sarbanes-Oxley Act. Section 404(b) of the Sarbanes-Oxley Act also requires our independent auditors to attest to, and report on, this management assessment. Ensuring that we have adequate internal controls in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will need to be evaluated frequently. If we are not able to comply with the requirements of Section 404 or if we or our independent registered public accounting firm are unable to attest to the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities, which would require additional financial and management resources.

Changes to healthcare and FDA laws, regulations, and policies may have a material adverse effect on our business and results of operations.

United States

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs and to modify the regulation of drug and biologic products. For example, the Affordable Care Act, as amended, substantially changed the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Affordable Care Act, among other things, subjects biologic products to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, and establishes annual fees and taxes on manufacturers of certain branded prescription drugs. A federal district court ruled the entire Affordable Care Act to be unconstitutional in December 2018, but issued a stay, meaning the law will remain in effect while the ruling is appealed. Implementation of the Affordable Care Act remains ongoing, but there is uncertainty as to how the law's various provisions will ultimately affect the industry and whether the law will remain in place.

Other legislative changes have been adopted in the United States, including the Cures Act and the Budget Control Act of 2011, or the Budget Act, signed into law on August 2, 2011. The Cures Act introduced a wide range of reforms and the Budget Act, among other things, required reductions in federal spending, which eventually triggered Medicare sequestration—the requirement to reduce Medicare payments to providers up to 2% per fiscal year. In 2013, the 2% Medicare payment reductions were applied to fee-for-service claims with dates of service or dates of discharge on or after April 1, 2013. Sequestration was initially set to expire in fiscal year 2021 but has been extended to 2025.

We expect that additional state and federal healthcare reform measures and regulations will be adopted in the future, including proposals to reduce the exclusivity protections provided to already approved biological products and to provide biosimilar and interchangeable biologic products an easier path to approval. Any of these measures and regulations could limit the amounts that federal and state governments will pay for healthcare products and services, result in reduced demand for our product candidates or additional pricing pressures and affect our product development, testing, marketing approvals and post-market activities.

EU

In the EU, the European Commission has adopted detailed rules for the safety features appearing on the packaging of medicinal products for human use. The regulations set forth the rules for the features appearing on the packaging of these medicinal products, including, inter alia, the characteristics and technical specifications of the unique identifier that enables the authenticity of medicinal products to be verified and individual packs to be identified, the modalities for the verification of the safety features, and the list of medicinal products and product categories subject and not subject to prescription which shall not bear and bear (respectively) safety features.

The European Commission has also launched a series of public consultations that are aimed at the adoption of notices and guidelines which will serve the interpretation of currently applicable regulations and directives. For example, between August 2015 and December 2016, the European Commission launched public consultations which concerned good manufacturing practices, clinical trials for human medicinal products, and orphan medicinal products. The purpose of the consultation on orphan medicinal products (which will be replaced with a Notice) is to streamline the regulatory framework and to adapt the applicable regulations to technical progress. The consultation focuses on a variety of elements of Regulation (EC) No 141/2000, which include the encouragement of development of orphan medicinal products for communicable diseases and the simplification of the procedure for the reassessment of orphan criteria when two authorization application procedures are pending in parallel for two orphan medicinal products.

We are subject, directly and indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Our operations are directly, and indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician sunshine laws and regulations. These laws impact, among other things, our field marketing and education programs. In addition, we are subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate, including the EU General Data Protection Regulation, are described in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019. Further, in the United States, California recently enacted the California Consumer Privacy Act (CCPA), which became effective on January 1, 2020. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. We may also incur increased costs as a result of complying with new legislations such as the CCPA.

International expansion of our business exposes us to business, regulatory, political, operational, financial, and economic risks associated with doing business outside of the United States.

Our business strategy includes international expansion. We currently conduct clinical studies and regulatory activities and we also commercialize products outside of the United States. Doing business internationally involves a number of risks, including but not limited to:

- multiple, conflicting, and changing laws and regulations such as privacy and data regulations, transparency regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;
- introduction of new health authority requirements and/or changes in health authority expectations;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining protection for, and enforcing, our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits on our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations;
- natural disasters and political and economic instability, including wars, terrorism, political unrest, results of certain elections and votes, actual or threatened public health emergencies and outbreak of disease (including for example, the COVID-19 pandemic), boycotts, adoption or expansion of government trade restrictions, and other business restrictions;
- certain expenses including, among others, expenses for travel, translation, and insurance;
- regulatory and compliance risks that relate to maintaining accurate information and control over commercial operations and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, or FCPA, its books and records provisions, or its anti-bribery provisions, including those under the U.K. Bribery Act and similar foreign laws and regulations; and
- regulatory and compliance risks relating to doing business with any entity that is subject to sanctions administered by the Office of Foreign Assets Control of the U.S. Department of the Treasury.

Any of these factors could significantly harm our future international expansion and operations and, consequently, our results of operations.

We may incur additional tax liabilities related to our operations.

We have a multinational tax structure and are subject to income tax in the United States and various foreign jurisdictions. Our effective tax rate is influenced by many factors including changes in our operating structure, changes in the mix of our earnings among countries, our allocation of profits and losses among our subsidiaries, our intercompany transfer pricing agreements and rules relating to transfer pricing, the availability of U.S. research and development tax credits, and future changes in tax laws and regulations in the U.S. and foreign countries. Significant judgment is required in determining our tax liabilities including management's judgment for uncertain tax positions. The Internal Revenue Service, other domestic taxing authorities, or foreign taxing authorities may disagree with our interpretation of tax laws as applied to our operations. Our reported effective tax rate and after-tax cash flows may be materially and adversely affected by tax assessments in excess of amounts accrued for our financial statements. This could materially increase our future effective tax rate thereby reducing net income and adversely impacting our results of operations for future periods.

Failure to comply with laws and regulations could harm our business and our reputation.

Our business is subject to regulation by various federal, state, local and foreign governmental agencies, including agencies responsible for monitoring and enforcing employment and labor laws, workplace safety, and tax laws and regulations. In certain jurisdictions, these regulatory requirements may be more stringent than those in the United States, and in other circumstances these requirements may be more stringent in the United States. Noncompliance with applicable regulations or requirements could subject us to investigations, sanctions, mandatory recalls, enforcement actions, disgorgement of profits, fines, damages, civil and criminal penalties, or injunctions. If any governmental sanctions, fines or penalties are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, operating results, financial condition and our reputation could be harmed. In addition, responding to any action will likely result in a significant diversion of management's attention and resources and an increase in professional fees. Enforcement actions and sanctions could further harm our business, operating results, financial condition, and our reputation.

In particular, our research and development activities and our and our third-party manufacturers' and suppliers' activities involve the controlled storage, use, and disposal of hazardous materials, including the components of our product candidates, such as viruses, and other hazardous compounds, which subjects us to laws and regulations governing such activities. In some cases, these hazardous materials and various wastes resulting from their use are stored at our or our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts, and business operations or environmental damage that could result in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. We cannot guarantee that the safety procedures utilized by us and our third-party manufacturers for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages—and such liability could exceed our resources—and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently, and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. We do not currently carry biological or hazardous waste insurance coverage.

Risks generally associated with a company-wide implementation of an enterprise resource planning (ERP) system may adversely affect our business and results of operations or the effectiveness of our internal controls over financial reporting.

We are in the process of implementing a company-wide ERP system to upgrade certain existing business, operational, and financial processes. Our ERP implementation is a complex and time-consuming project that we expect will require multiple years to complete. Our results of operations could be adversely affected if we experience time delays or cost overruns during the ERP implementation process, or if the ERP system or associated process changes do not give rise to the benefits that we expect. This project has required and may continue to require investment of capital and human resources, the re-engineering of processes of our business, and the attention of many employees who would otherwise be focused on other aspects of our business. Any deficiencies in the design and implementation of the new ERP system could result in potentially much higher costs than we had incurred and could adversely affect our ability to develop and launch solutions, provide services, fulfill contractual obligations, file reports with the SEC in a timely manner, operate our business or otherwise affect our controls environment. Any of these consequences could have an adverse effect on our results of operations and financial condition.

Our business and operations may be materially adversely affected in the event of computer system failures or security breaches.

Despite the implementation of security measures, our internal computer systems, and those of our CROs and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, cyber-attacks, natural disasters, fire, terrorism, war, and telecommunication and electrical failures. Risks of unauthorized access and cyber-attacks have increased as most of our personnel, and the personnel of many third-parties with which we do business, have adopted remote working arrangements as a result of the COVID-19 pandemic. Improper or inadvertent employee behavior, including data privacy breaches by employees, contractors and others with permitted access to our systems, may also pose a risk that sensitive data may be exposed to unauthorized persons or to the public. If a system failure or security breach occurs and interrupts our operations or the operations at one of our third-party vendors, it could result in intellectual property and other proprietary or confidential information being lost or stolen or a material disruption of our drug development programs. For example, the loss of clinical trial data from ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, loss of trade secrets or inappropriate disclosure of confidential or proprietary information, including protected health information or personal data of employees or former employees, access to our clinical data, or disruption of the manufacturing process, we could incur liability and the further development of our drug candidates could be delayed. We may also be vulnerable to cyber-attacks by hackers or other malfeasance. This type of breach of our cybersecurity may compromise our confidential information and/or our financial information and adversely affect our business or reputation or result in legal or regulatory proceedings.

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters and one of our laboratories are located in the San Francisco Bay Area, and our collaboration partner for Crysvita, KKC, is located in Japan, which have both in the past experienced severe earthquakes and other natural disasters. We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations or those of our collaborators, and have a material adverse effect on our business, results of operations, financial condition, and prospects. If a natural disaster, power outage, or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure (such as the manufacturing facilities of our third-party contract manufacturers) or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are may be inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

We may acquire companies or products or engage in strategic transactions, which could divert our management's attention and cause us to incur various costs and expenses, or result in fluctuations with respect to the value of such investment, which could impact our operating results.

We may acquire or invest in businesses or products that we believe could complement or expand our business or otherwise offer growth opportunities. For example, we acquired Dimension in November 2017 and during the third quarter 2019, we entered into an agreement with GeneTx to collaborate on the development of a product for the treatment of Angelman Syndrome which included an exclusive option to acquire GeneTx. The pursuit of potential acquisitions or investments may divert the attention of management and may cause us to incur various costs and expenses in identifying, investigating, and pursuing them, whether or not they are consummated. We may not be able to identify desirable acquisitions or investments or be successful in completing or realizing anticipated benefits from such transactions. In addition, we may receive inquiries relating to potential strategic transactions, including collaborations, licenses, and acquisitions. Such potential transactions may divert the attention of management and may cause us to incur various costs and expenses in investigating and evaluating such transactions, whether or not they are consummated.

The value of our investments in other companies or businesses may also fluctuate significantly and impact our operating results quarter to quarter or year to year. For instance, in June 2019, we purchased 2.4 million shares of common stock of Arcturus Therapeutics Holdings, Inc. (Arcturus) and in May 2020, we exercised our option to purchase an additional 600,000 shares of Arcturus' common stock pursuant to the terms of our equity purchase agreement with Arcturus. We have elected to apply the fair value option to account for our equity investments in Arcturus. As a result, increases or decreases in the stock price of Arcturus common stock will result in accompanying changes in the fair value of our investments and impact, and cause substantial volatility in, our operating results for the reporting period. For instance, the increases in fair value of the Arcturus investments recognized in the Condensed Consolidated Statements of Operations for the three and six months ended June 30, 2020 were $95.2 million and $102.9 million, respectively, primarily due to the higher Arcturus stock price at June 30, 2020 compared to December 31, 2019. Such gain in fair value of the investment resulted in net income for the three months ended June 30, 2020 and decreased the amount of our net loss for the six months ended June 30, 2020. If the Arcturus stock price had been lower at June 30, 2020 compared to December 31, 2019, we may have reported a net loss for the quarter and an even greater net loss for the six months ended June 30, 2020. As the fair value of our investment in Arcturus is dependent on the stock price of Arcturus, which has recently seen wide fluctuations, the value of our investments and the impact on our operating results may similarly fluctuate significantly from quarter to quarter and year to year such that period-to-period comparisons may not be a good indication of the future value of the investments and our future operating results.

Litigation may substantially increase our costs and harm our business.

We have been, and may in the future become, party to lawsuits including, without limitation, actions and proceedings in the ordinary course of business relating to our directors, officers, stockholders, intellectual property, and employment matters, which will cause us to incur legal fees and other costs related thereto, including potential expenses for the reimbursement of legal fees of officers and directors under indemnification obligations. The expense of defending against such litigation may be significant and there can be no assurance that we will be successful in any defense. Further, the amount of time that may be required to resolve such lawsuits is unpredictable, and these actions may divert management's attention from the day-to-day operations of our business, which could adversely affect our business, results of operations, and cash flows. Litigation is subject to inherent uncertainties, and an adverse result in such matters that may arise from time to time could have a material adverse effect on our business, results of operations, and financial condition.

Risks Related to Ownership of Our Common Stock

The market price of our common stock may be highly volatile.

The market price of our common stock has been, and is likely to continue to be, volatile, including for reasons unrelated to changes in our business. Our stock price could be subject to wide fluctuations in response to a variety of factors, including but not limited to the following:

- adverse results or delays in preclinical or clinical studies;
- any inability to obtain additional funding;
- any delay in filing an IND, NDA, BLA, MAA, or other regulatory submission for any of our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory agency's review of that IND, NDA, BLA, MAA, or other regulatory submission;
- the perception of limited market sizes or pricing for our products and product candidates;
- decisions by our collaboration partners with respect to the indications for our products and product candidates in countries where they have the right to commercialize the products and product candidates;
- decisions by our collaboration partners regarding market access and pricing in countries where they have the right to commercialize our products and product candidates;
- failure to successfully develop and commercialize our products and product candidates;
- the level of revenue we receive from our commercialized products or from named patient sales;
- post-marketing safety issues;
- failure to maintain our existing strategic collaborations or enter into new collaborations;
- failure by us or our licensors and strategic collaboration partners to prosecute, maintain, or enforce our intellectual property rights;
- changes in laws or regulations applicable to our products;
- any inability to obtain adequate product supply for our products and product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services, or technologies by our competitors;

- changes in or failure to meet or exceed financial projections or other guidance we may provide to the public;
- changes in or failure to meet or exceed the financial projections or other expectations of the investment community;
- the perception of the pharmaceutical industry or our company by the public, legislatures, regulators, and the investment community;
- the perception of the pharmaceutical industry's approach to drug pricing;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us, our strategic collaboration partners, or our competitors;
- the integration and performance of any businesses we have acquired or may acquire;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- securities or industry analysts' reports regarding our stock, or their failure to issue such reports;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions, including the impact from the COVID-19 pandemic;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

In addition, biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities, or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities, or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to our 2014 Incentive Plan, or the 2014 Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors, and consultants. At June 30, 2020, 3,304,531 shares were available for future grants under the 2014 Plan. Through January 1, 2024, the number of shares available for future grant under the 2014 Plan will automatically increase on January 1 of each year by the lesser of 2,500,000 shares or 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our compensation committee to take action to reduce the size of the increase in any given year.

Pursuant to our 2014 Employee Stock Purchase Plan, or 2014 ESPP, eligible employees can acquire shares of our common stock at a discount to the prevailing market price. At June 30, 2020, 3,287,825 shares were available for issuance under the 2014 ESPP. Through January 1, 2024, the number of shares available for issuance under the 2014 ESPP will automatically increase on January 1 of each year by the lesser of 1,200,000 shares or 1% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our compensation committee to take action to reduce the size of the increase in any given year.

Currently we plan to register the increased number of shares available under the 2014 Plan and the 2014 ESPP each year. If our board of directors elects to increase the number of shares available for future grant under the 2014 Plan or the 2014 ESPP, our stockholders may experience additional dilution, which could cause our stock price to fall.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history. To the extent that we continue to generate taxable losses, unused taxable losses will, subject to certain limitations, carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the IRC, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOL carryforwards, and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. An analysis to determine limitations upon our NOL carryforwards and other pre-change tax attributes for ownership changes that have occurred previously has been performed, resulting in a permanent decrease of federal and state NOL carryforwards in the amount of $7.2 million and a permanent decrease in federal research tax credit carryforwards in the amount of $0.2 million. As a result of these decreases and others that may occur as a result of future ownership changes, our ability to use our pre-change NOL carryforwards and other tax attribute carryforwards to offset U.S. federal taxable income and tax liabilities is limited and may become subject to even greater limitations, which could potentially accelerate or permanently increase future federal tax liabilities for us. In addition, there may be periods during which the use of state income tax NOL carryforwards and other state tax attribute carryforwards (such as state research tax credits) are suspended or otherwise limited, which could potentially accelerate or permanently increase future state tax liabilities for us.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings, if any, for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

Provisions in our amended and restated certificate of incorporation and by-laws, as well as provisions of Delaware law, could make it more difficult for a third-party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, or remove our current management.

Our amended and restated certificate of incorporation, amended and restated by-laws, and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our amended and restated certificate of incorporation and by-laws include provisions that:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend, and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors or the chairperson of our board of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a resolution adopted by the board of directors;
- expressly authorize our board of directors to modify, alter or repeal our amended and restated by-laws; and
- require holders of 75% of our outstanding common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by-laws.

These provisions, alone or together, could delay, deter, or prevent hostile takeovers and changes in control or changes in our management.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Further, no stockholder is permitted to cumulate votes at any election of directors because this right is not included in our amended and restated certificate of incorporation.

Any provision of our amended and restated certificate of incorporation or amended and restated by-laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the sole and exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, or other employees to us or to our stockholders, (3) any action asserting a claim against us arising under the Delaware General Corporation Law or under our amended and restated certificate of incorporation or bylaws, or (4) any action against us asserting a claim governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage such lawsuits against us and our directors, officers, and other employees. Alternatively, if a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, operating results and financial condition.

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

None.

Item 3. ***Defaults Upon Senior Securities***

None.

Item 4. ***Mine Safety Disclosures***

Not applicable.

Item 5. ***Other Information***

None.

Item 6. ***Exhibits***

		Incorporated by Reference			
Exhibit Number	**Exhibit Description**	**Form**	**Date**	**Number**	**Furnished or Filed Herewith**
3.1	Amended and Restated Certificate of Incorporation	8-K	2/5/2014	3.1	
3.2	Amended and Restated Bylaws	8-K	2/5/2014	3.2	
10.1	Equity Purchase Agreement, dated as of June 18, 2019 by and among Ultragenyx Pharmaceutical Inc. and Arcturus Therapeutics Ltd.				X
10.2	Third Amendment, dated as of July 29, 2019, to the Lease Agreement dated as of October 30, 2015 by and between Ultragenyx Pharmaceutical Inc. and ARE-MA Region No., LLC.				X
10.3	Fourth Amendment, dated as of March 31, 2020, to the Lease Agreement dated as of October 30, 2015 by and between Ultragenyx Pharmaceutical Inc. and ARE-MA Region No., LLC.				X
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act				X
31.2	Certification of Principal Financial Officer Required Under Rule 13a-14(a) or Rule 15d-14(a) of the Exchange Act				X
32.1*	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) or Rule 15d-14(b) of the Exchange Act and 18 U.S.C. 1350				X
101.INS	XBRL Instance Document, formatted in Inline XBRL				X
101.SCH	Inline XBRL Taxonomy Extension Schema Document				X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document				X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				X
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document				X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document				X
104	The cover page from the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2020, formatted in Inline XBRL (included in Exhibit 101).				

* The certification attached as Exhibit 32.1 that accompanies this Quarterly Report is furnished to, and not deemed filed with, the SEC and is not to be incorporated by reference into any filing of the Registrant under the Securities Act or the Exchange Act, whether made before or after the date of this Form 10-Q, irrespective of any general incorporation language contained in such filing.

SIGNATURES

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

ULTRAGENYX PHARMACEUTICAL INC.

Date: July 30, 2020

By: /s/ Emil D. Kakkis
Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Duly Authorized Officer)

Date: July 30, 2020

By: /s/ Shalini Sharp
Shalini Sharp
Executive Vice President and Chief Financial Officer
(Principal Financial Officer)

Date: July 30, 2020

By: /s/ Theodore A. Huizenga
Theodore A. Huizenga
Senior Vice President and Corporate Controller
(Principal Accounting Officer)

Exhibit 10.1

EQUITY PURCHASE AGREEMENT

THIS EQUITY PURCHASE AGREEMENT (this "***Agreement***") is made as of June 18, 2019, by and among Ultragenyx Pharmaceutical Inc., a Delaware corporation (the "***Investor***"), Arcturus Therapeutics Ltd., an Israeli incorporated company ("***Arcturus-Israel***"), and Arcturus Therapeutics Holdings Inc., a newly incorporated Delaware corporation ("***Arcturus-Delaware***").

WHEREAS, on June 18, 2019 (the "***Effective Date***"), the Company's wholly-owned subsidiary, Arcturus Therapeutics, Inc., a Delaware corporation ("***Arcturus***"), and the Investor entered into Amendment No. 3 (the "***Amendment***") to the Research Collaboration and License Agreement, dated as of October 26, 2015 (the "***Collaboration Agreement***"), by and between Arcturus and the Investor;

WHEREAS, on June 12, 2019, Arcturus-Israel exchanged all its outstanding ordinary shares, par value NIS 0.07 per share, of Arcturus-Israel, for shares of common stock, par value $0.001 per share ("***Common Stock***"), of Arcturus-Delaware in connection with the redomicile of Arcturus-Israel from Israel to the State of Delaware pursuant to the terms of an Exchange Agreement entered into by Arcturus-Delaware and Arcturus-Israel on February 8, 2019, (the "***Redomiciliation***");

WHEREAS, as contemplated by the Amendment and pursuant to the terms and subject to the conditions set forth in this Agreement, the Company desires to issue and sell to the Investor, and the Investor desires to subscribe for and purchase from the Company, at the Closing, 2,400,000 shares of Common Stock (the "***Shares***"), for a purchase price of $10.00 per share;

WHEREAS, as contemplated by the Amendment and pursuant to the terms and subject to the conditions set forth in this Agreement, the Company desires to grant to the Investor the right, but not the obligation, to purchase from the Company, at a subsequent closing on or before the second anniversary of the Effective Date (such date, as it may be extended pursuant to Section 3.1(b), the "***Expiration Date***"), up to 600,000 additional shares of Common Stock (the "***Additional Shares***") for a purchase price per Additional Share equal to the Additional Share Price; and

WHEREAS, the Company and the Investor are executing and delivering this Agreement in reliance upon the exemption from securities registration afforded by the provisions of Regulation D, as promulgated by the U.S. Securities and Exchange Commission (the "***Commission***") under the Securities Act of 1933, as amended (the "***Securities Act***").

NOW, THEREFORE, in consideration of the following mutual promises and obligations, and for good and valuable consideration, the adequacy and sufficiency of which are hereby acknowledged, the Investor, Arcturus-Israel and Arcturus-Delaware agree as follows:

1. **Definitions**.

1.1. **Defined Terms**. When used in this Agreement, the following terms shall have the respective meanings specified therefor below:

"*13D Group*" has the meaning set forth in Section 6.1(c).

"*Action*" means any civil, criminal or administrative litigation, claim, action, suit, arbitration, hearing, inquiry, investigation or other similar proceeding by or before any Governmental Authority.

"*Additional Closing*" has the meaning set forth in Section 3.2.

"*Additional Closing Date*" has the meaning set forth in Section 3.2.

"*Additional Closing Representations*" means the representations and warranties set forth in Sections 4.1, 4.2, 4.3 and 4.4.

"*Additional Share Price*" means $16.00, subject to adjustment as set forth in Section 9.1.

"*Additional Shares*" has the meaning set forth in the Recitals.

"*Affiliate*" means, with respect to a specified Person, any other Person which controls, is controlled by or is under common control with the applicable Person. As used herein, "controls", "control" and "controlled" means the possession, direct or indirect, of the power to direct the management and policies of a Person, whether through the ownership of voting interests of such Person, through contract or otherwise; provided that the Company and its subsidiaries shall not be deemed Affiliates of the Investor or its subsidiaries.

"*Affiliated Persons*" has the meaning set forth in Section 6.7(f).

"*Aggregate Purchase Price*" has the meaning set forth in Section 2.1.

"*Agreement*" has the meaning set forth in the Preamble.

"*Amendment*" has the meaning set forth in the Recitals.

"*Applicable SEC Documents*" has the meaning set forth in Section 4.7(a).

"*Arcturus*" has the meaning set forth in the Recitals.

"*Arcturus-Delaware*" has the meaning set forth in the Preamble.

"*Arcturus-Israel*" has the meaning set forth in the Preamble.

"*Business Day*" means a day on which commercial banking institutions in San Diego, California and New York, New York are open for business.

"*Change of Control*" has the meaning set forth in Section 6.3(a)(i).

"*Closing*" has the meaning set forth in Section 2.2.

"*Closing Date*" has the meaning set forth in Section 2.2.

"*Collaboration Agreement*" has the meaning set forth in the Recitals.

"*Commission*" has the meaning set forth in the Recitals.

"*Common Stock*" has the meaning set forth in the Recitals.

"*Company*" means, prior to the Redomiciliation, Arcturus-Israel, and, after the Redomiciliation, Arcturus-Delaware.

"*Company Equity Plans*" means (i) the Company's 2018 Omnibus Equity Incentive Plan, (ii) the Company's 2013 Equity Incentive Plan, (iii) the Company's 2010 Incentive Option Plan and (iv) the Company's 2019 Omnibus Equity Incentive Plan.

"*Company Fundamental Representations*" has the meaning set forth in Section 7.1(a).

"*Company Securities*" has the meaning set forth in Section 4.5(a).

"*Company Studies and Trials*" has the meaning set forth in Section 4.24(b).

"*Continuing Directors*" means the directors of the Company on the date hereof, and each other director, if, in each case, such other director's nomination for election to the Company's board of directors was recommended by, or whose appointment to the Company's board of directors was approved by, at least a majority of the other Continuing Directors.

"*Controlling Stake*" has the meaning set forth in Section 6.3(c).

"*Covered Person*" has the meaning set forth in Section 4.15.

"*Effective Date*" has the meaning set forth in the Recitals.

"*Environmental Laws*" means any Laws relating to the protection of human health and safety, the environment or hazardous or toxic substances or wastes, pollutants or contaminants.

"*Equitable Exceptions*" has the meaning set forth in Section 4.2.

"*Exchange Act*" means the Securities Exchange Act of 1934, as amended.

"*Exercise Notice*" has the meaning set forth in Section 3.2.

"*Expiration Date*" has the meaning set forth in the Recitals.

"*Financial Statements*" has the meaning set forth in Section 4.7(a).

"*GAAP*" means United States generally accepted accounting principles.

"*Governmental Authority*" means any applicable government authority, court, tribunal, arbitrator, agency, department, legislative body, commission, regulatory or administrative authority or other instrumentality of (a) any government of any country or territory, (b) any nation, state, province, county, city or other political subdivision thereof, (c) any supranational body or

(d) any self-regulatory organization.

"*Initial Designee*" has the meaning set forth in Section 6.7(a).

"*Intellectual Property Assets*" has the meaning set forth in Section 4.24(a).

"*Intellectual Property Rights*" has the meaning set forth in Section 4.24(a).

"*Investor*" has the meaning set forth in the Preamble.

"*Investor Designee*" has the meaning set forth in Section 6.7(a).

"*Investor Fundamental Representations*" has the meaning set forth in Section 7.2(a).

"*Investor Observer*" has the meaning set forth in Section 6.7(a).

"*Investor Party*" has the meaning set forth in Section 6.5(a).

"*Law*" or "*Laws*" means any federal, national, supranational, state, provincial, local or similar laws, statutes, rules, codes, regulations, writs, orders, judgments, decrees, injunctions, awards, executive orders, rulings and/or ordinances of any Governmental Authority, including any common law.

"*Liens*" means all pledges, liens (including environmental and tax liens), restrictions on transfer, preemptive rights, charges, mortgages, encumbrances, security interests, conditional and installment sale agreements or other claims of third parties or restrictions of any kind whatsoever, including any easement, reversion interest, right of way or other encumbrance to title, limitations on voting rights, or any option, right of first refusal or right of first offer.

"*Material Adverse Effect*" means any event, change, fact, development, occurrence or effect (each, an "*Effect*") that, individually or collectively with one or more other Effects, (a) has had a material adverse effect on the business, assets, liabilities, financial condition, prospects or results of operations of the Company and its Subsidiaries, taken as a whole or (b) prevents or materially delays the ability of the Company to perform its obligations under, or consummate, the transactions contemplated by, this Agreement; provided that, solely for purposes of clause (a) of this definition, none of the following matters, either alone or in combination, will constitute, or be considered in determining whether there has been, a Material Adverse Effect: (i) any outbreak or escalation of war or major armed hostilities or any act of terrorism, (ii) changes in applicable laws, rules, regulations or GAAP after the date of this Agreement, (iii) changes that generally affect the industry in which the Company operates, (iv) changes in financial markets, general economic conditions or political conditions, (v) changes in the trading price or trading volume of the Common Stock, and (vi) failure by the Company to meet any published or internally prepared projections, budgets, plans or forecasts of revenues, earnings or other financial performance measures or operating statistics, except, in the case of clauses (i) through (iv), to the extent those Effects have a disproportionate effect on the Company and its Subsidiaries, taken as a whole, as compared to other similarly situated companies operating in the industry in which the Company and its Subsidiaries operate, and with respect to clauses (v) and (vi), it being understood that the facts and circumstances underlying any such change or failure that are not otherwise expressly

excluded in clauses (i) through (vi) herein from the definition of a "Material Adverse Effect" may be considered in determining whether there has been a Material Adverse Effect.

"*Material Contract*" has the meaning set forth in Section 4.12.

"*Money Laundering Laws*" has the meaning set forth in Section 4.19.

"*Nasdaq*" has the meaning set forth in Section 4.2(b).

"*Offered Securities*" has the meaning set forth in Section 6.4.

"*Organizational Documents*" means (i) with respect to Arcturus Therapeutics Ltd., the Articles of Association of Arcturus Therapeutics Ltd., filed on November 30, 2017, and all bylaws of Arcturus Therapeutics Ltd., and (ii) with respect to Arcturus-Delaware, the Certificate of Incorporation of Arcturus-Delaware and the Bylaws of Arcturus-Delaware, in the forms attached as Exhibit B and Exhibit C, respectively, to the Company's Registration Statement on Form S-4, filed on April 11, 2019.

"*Permits*" has the meaning set forth in Section 4.26(c).

"*Permitted Issuance*" has the meaning set forth in Section 3.5(a).

"*Person*" means any individual, partnership, limited liability company, firm, corporation, association, trust, unincorporated organization, government or any department or agency thereof or other entity, as well as any syndicate or group that would be deemed to be a Person under Section 13(d)(3) of the Exchange Act.

"*Preferred Stock*" has the meaning set forth in Section 4.5(a).

"*Redomiciliation*" has the meaning set forth in the Recitals.

"*Registration Rights Agreement*" has the meaning set forth in Section 2.3.

"*Replacement Designee*" has the meaning set forth in Section 6.7(a).

"*Rule 144*" means Rule 144 promulgated under the Securities Act.

"*Rule 506*" has the meaning set forth in Section 4.21.

"*Sanctions*" has the meaning set forth in Section 4.18.

"*SEC Reports*" has the meaning set forth in Section 4.

"*Securities Act*" has the meaning set forth in the Recitals.

"*Shares*" has the meaning set forth in the Recitals.

"*Significant Event*" has the meaning set forth in Section 6.3(c).

"*Special Committee*" has the meaning set forth in Section 6.7(c).

"*Stock Event*" has the meaning set forth in Section 9.1.

"*Subsidiary*" of any Person means any corporation, limited liability company, partnership, limited partnership, association, trust, unincorporated organization or other legal entity of which such Person (either alone or through or together with any other Subsidiary) owns, directly or indirectly, a majority of the stock or other equity interests, the holders of which are generally entitled to vote for the election of the board of directors or other governing body of such corporation or other legal entity, or any Person that would otherwise be deemed a "subsidiary" under Rule 12b 2 promulgated under the Exchange Act.

"*Termination Date*" has the meaning set forth in Section 8.1(b).

"*Third Party*" means any Person (other than a Governmental Authority) other than the Investor, the Company or any Affiliate of the Investor or the Company.

"*Threshold*" has the meaning set forth in Section 3.1(b).

"*Total Voting Power*" has the meaning set forth in Section 6.3(a)(i).

"*Transaction*" means the issuance and sale of the Shares by the Company, and the purchase of the Shares by the Investor, in accordance with the terms hereof.

"*Transfer*" has the meaning set forth in Section 6.2.

"*Transfer Agent*" has the meaning set forth in Section 2.3.

2. **Purchase and Sale of Shares**.

2.1. **Shares**. Subject to the terms and conditions of this Agreement, at the Closing, the Company shall issue and sell to the Investor and the Investor shall purchase from the Company, the Shares at a cash purchase price of $10.00 per share for an aggregate purchase price of $24,000,000 (the "***Aggregate Purchase Price***").

2.2. **Closing Date**. The closing of the purchase and sale of the Shares hereunder (the "***Closing***") shall occur remotely via the exchange of documents and signatures on the third Business Day after all conditions for Closing set forth in Section 7 have been satisfied or, to the extent permitted, waived (other than those conditions that by their nature are to be satisfied at the Closing, but subject to their satisfaction or, to the extent permitted, waiver at the Closing), or at such other time, date and location as the Company and the Investor may mutually agree in writing. The date the Closing occurs is hereinafter referred to as the "***Closing Date***".

2.3. **Deliveries**. At the Closing, the Company shall deliver, or cause to be delivered, to the Investor the Shares in book-entry form, and the Company shall instruct its transfer agent for the shares of Common Stock (the "***Transfer Agent***") to register such issuance at the time of such issuance. At the Closing, the Investor shall deliver to the Company an amount in cash equal to the Aggregate Purchase Price, by wire transfer of immediately available funds to a bank account

designated in writing by the Company not less than two (2) Business Days before the Closing Date. At or prior to the Closing, the Company and the Investor shall execute and deliver the Registration Rights Agreement, in the form attached hereto as Exhibit A (the "***Registration Rights Agreement***"), and any related agreements or other documents required to be executed hereunder or reasonably requested by the other party hereto.

3. **Purchase and Sale of Additional Shares**.

3.1. **Additional Shares**.

(a) During the period beginning on the Closing Date and ending on the Expiration Date, the Investor shall have the right, but not the obligation, to purchase, and to direct the Company to issue and sell to the Investor, by its delivery to the Company of an Exercise Notice, the Additional Shares. Upon delivery to the Company of an Exercise Notice, the Investor shall have the obligation to purchase, and the Company shall have the obligation to sell to the Investor, the Additional Shares, subject to the terms and conditions set forth in this Agreement, including Section 3.1(b).

(b) Notwithstanding the foregoing provisions of Section 3.1(a), in the event purchasing all of the Additional Shares would result in Investor and its Affiliates owning in excess of 19.99% of the then-issued and outstanding shares of Common Stock immediately after giving effect to such purchase (the "***Threshold***"), Investor shall only be entitled to purchase that number of Additional Shares that would result in Investor and its Affiliates owning a number of shares of Common Stock equal to the Threshold. In the event that the Investor is not permitted to purchase all of the Additional Shares due to the foregoing sentence, (A) the Expiration Date shall be extended until the earlier of (x) such time as the Investor may purchase any remaining portion of the Additional Shares and (y) the fourth anniversary of the Effective Date and (B) the Investor shall be permitted to submit one or more additional Exercise Notices to effect the purchase of the Additional Shares not purchased as a result of the first sentence of this Section 3.1(b). Any Additional Shares not purchased by the Investor are referred to herein as the "***Additional Unpurchased Shares***."

(c) Within two (2) Business Days (i) after the end of each month prior to the earlier of (A) the Expiration Date and (B) the date on which all Additional Shares have been purchased by the Investor, and (ii) after a request by the Investor for such information, the Company shall deliver to the Investor a written statement indicating (x) the number of shares of Common Stock issued and outstanding on such date and (y) the number of Additional Unpurchased Shares that the Investor would be permitted to purchase without exceeding the Threshold.

(d) Notwithstanding the Threshold, in the event there are Additional Unpurchased Shares as of immediately prior to the closing of a Change of Control, then, immediately prior to the Closing of a Change of Control in circumstances where the fair market value of the consideration to be received in respect of a share of Common Stock in such Change of Control as reasonably determined in good faith by the Company's board of directors (the "***Fair Market Value***") is in excess of the Additional Share Price, the Company shall issue to the Investor (i) a number of whole shares of Common Stock equal to (x) the number of Additional Unpurchased

Shares as of immediately prior to the closing of a Change of Control, reduced by (y) that number of shares of Common Stock equal to the quotient obtained by dividing (A) the product of (1) the Additional Share Price multiplied by (2) the Additional Unpurchased Shares as of immediately prior to the closing of a Change of Control by (B) the Fair Market Value, and (ii) cash in lieu of any fractional shares (based on the Fair Market Value).

3.2. **Exercise Notice**. The term "***Exercise Notice***" shall mean an irrevocable written notice specifying a closing date for the purchase of Additional Shares pursuant to Section 3.1 (an "***Additional Closing***"), which notice shall be delivered at least five (5) Business Days prior to the date of the applicable Additional Closing. The date on which an Additional Closing occurs is hereinafter referred to as an "***Additional Closing Date***".

3.3. **Additional Closing**. At an Additional Closing (or one or more Additional Closings if permitted by Section 3.1(b)), which shall take place on the date specified in the applicable Exercise Notice, (a) the Company shall (i) deliver the Investor a certificate (an "***Additional Closing Certificate***"), dated as of the Additional Closing Date, executed by a duly authorized officer of the Company, certifying that the Additional Closing Representations are true and correct on the Additional Closing Date, (ii) deliver, or cause to be delivered, to the Investor the Additional Shares to be purchased at such Additional Closing in book-entry form, and (iii) instruct the Transfer Agent to register such issuance at the time of such issuance, and (b) the Investor shall deliver to the Company an amount in cash equal to the product of (i) the number of Additional Shares to be purchased pursuant to such Exercise Notice (subject to Section 3.1(b)) and (ii) the Additional Share Price, by wire transfer of immediately available funds to a bank account designated in writing by the Company not less than two (2) Business Days before such Additional Closing Date. At or prior to an Additional Closing, the Company and the Investor shall execute any related agreements or other documents required to be executed hereunder or reasonably requested by the other party hereto.

3.4. **Beneficial Ownership Limitation**. Notwithstanding anything herein to the contrary, if at any time the shares of Common Stock beneficially owned by Investor and its Affiliates constitute in excess of the Threshold because the number of issued and outstanding shares of Common Stock or other Company Securities is reduced by any action taken by or on behalf of the Company, including as a result of a Stock Event, the Investor and its Affiliates shall not be required to dispose of any of their holdings of Company Securities.

3.5. **Subsequent Equity Sales**.

(a) Except as required pursuant to this Agreement, from the date hereof until ninety (90) days after the Closing Date, without the consent of the Investor, the Company shall not issue any Company Securities. Notwithstanding the foregoing sentence, the provisions of this Section 3.5(a) shall not apply to (i) the issuance of the Shares or Additional Shares hereunder, (ii) the issuance of shares of Common Stock upon the conversion or exercise of any Company Securities outstanding on the date hereof or outstanding pursuant to clause (iii) or (iv) of this paragraph, (iii) the issuance of any Company Securities pursuant to the Company Equity Plans, or (iv) the filing of a registration statement under the Securities Act to register the offer and sale of securities on a newly adopted stock-based compensation plan or (v) the issuance of up to 2,000,000 shares of Common Stock for a price per share that is equal to or greater than $10.00 per share (or

otherwise consented to by the Investor) to one or more institutional investors in a private placement or public offering (each of clauses (i), (ii) (iii), (iv) and (v), a "***Permitted Issuance***").

(b) The Company shall not sell, offer for sale or solicit offers to buy or otherwise negotiate in respect of any security (as defined in Section 2 of the Securities Act) that will be integrated with the offer or sale of the Shares or Additional Shares in a manner that would require the registration under the Securities Act of the sale of the Shares or Additional Shares to the Investor, or that will be integrated with the offer or sale of the Shares or Additional Shares for purposes of the rules and regulations of any trading market such that it would require stockholder approval prior to the Closing or an Additional Closing, as applicable, unless stockholder approval is obtained before the closing of such subsequent transaction.

4. **Representations and Warranties of the Company**. Except as disclosed in the Applicable SEC Documents that are publicly available at least one (1) Business Day prior to the date of this Agreement or, solely for purposes of any Additional Closing Certificate, that are publicly available at least one (1) Business Day prior to the date of the applicable Exercise Notice (collectively, the "***SEC Reports***") (excluding any disclosures in the SEC Reports under the headings "Risk Factors" and "Forward-Looking Statements" and any other disclosures of risks explicitly included in any "forward-looking statements" disclaimer and any other disclosures included therein to the extent they are predictive and forward-looking in nature, in each case other than specific factual information contained therein), it being understood that any matter disclosed in the SEC Reports shall not be deemed disclosed for purposes of Sections 4.1, 4.2, 4.3, 4.4 and 4.5, the Company hereby represents and warrants, as of the date hereof and as of the Closing Date, to the Investor as follows:

4.1. **Organization and Standing**. Arcturus-Israel is an Israeli incorporated company, duly organized, validly existing and in good standing under the Laws of Israel, and Arcturus-Delaware is a Delaware corporation, duly organized, validly existing and in good standing under the Laws of the State of Delaware. The Company has full corporate power and authority to own, lease and operate its properties and conduct its business as presently conducted and intended to be conducted, as set forth in the SEC Reports, and is duly qualified or licensed as a foreign corporation to do business, and is in good standing, in all jurisdictions in which the character of the property owned, leased or operated by it or the nature of the business transacted by it makes qualification or licensing necessary, except where the failure to be so qualified or licensed has not had and could not reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect.

4.2. **Corporate Power; Authorization; No Conflict**.

(a) The Company has all requisite corporate power and authority, and has taken all requisite corporate action, to execute and deliver this Agreement and the Registration Rights Agreement, to consummate the transactions contemplated hereby and thereby and to perform all of its obligations hereunder and thereunder. Each of this Agreement and the Registration Rights Agreement has been duly and validly executed and delivered by the Company and constitutes the legal, valid and binding obligation of the Company, enforceable in accordance with its terms, except (i) as may be limited by applicable bankruptcy, insolvency, reorganization, moratorium or similar laws relating to or affecting the enforcement of creditors' rights generally, and (ii) as

limited by equitable remedies, including any specific performance (the "***Equitable Exceptions***").

(b) The execution and delivery of this Agreement and the Registration Rights Agreement does not, and the performance of this Agreement and the Registration Rights Agreement, the compliance with the provisions hereof and thereof, and the consummation of the transactions contemplated hereby and thereby will not, conflict with, or result in a breach, loss of right under or violation of the terms, conditions or provisions of, or constitute a default (or an event which, with notice or lapse of time or both, would become a default) under, or give to others any right of termination, amendment, acceleration or cancellation of, or result in the creation or imposition of any Lien pursuant to, (i) the Organizational Documents of the Company or any of its Subsidiaries, (ii) any Law (including the rules and regulations of The Nasdaq Global Market ("***Nasdaq***"), including Rule 5635) or Permit applicable to the Company or any of its Subsidiaries or by which any properties of the Company or its Subsidiaries is bound or affected, or (iii) the terms of any indenture, deed of trust, note, mortgage, lease or other agreement or instrument to which the Company or any of its Subsidiaries is a party or bound or to which any of their respective properties is subject. No approval of the shareholders of the Company or other corporate proceeding or Third Party approval or consent is required to authorize this Agreement or the Registration Rights Agreement, or for the Company to consummate the transactions contemplated hereby, including to issue and deliver to the Investor the Shares, or thereby.

4.3. **Organizational Documents**. The Organizational Documents that are on file with the Commission are current, complete and correct copies thereof as in effect on the date hereof. The Organizational Documents are in full force and effect. The Company is not in violation of any provisions of its Organizational Documents.

4.4. **Issuance and Delivery of the Shares**. The Shares and Additional Shares have been duly authorized and, when issued and paid for in compliance with the provisions of this Agreement, will be validly issued, fully paid and nonassessable and free and clear of any and all Liens. The issuance and delivery of the Shares and the Additional Shares is not subject to preemptive, co-sale, right of first refusal or any other similar rights of the shareholders of the Company.

4.5. **Capitalization**.

(a) The authorized share capital of the Company consists of 30,000,000 shares of Common Stock, and 10,000,000 shares of preferred stock, par value $0.001 per share ("***Preferred Stock***"). As of the date hereof, (i) 10,718,844 shares of Common Stock are issued and outstanding, all of which are duly authorized, validly issued, fully paid and nonassessable and were issued free of preemptive (or similar) rights, (ii) no shares of Common Stock are owned by the Company or its Subsidiaries, (iii) 1,436,933 shares of Common Stock are issuable upon the exercise of outstanding stock options or upon the settlement of outstanding equity awards issued pursuant to the Company Equity Plans, (iv) 1,163,067 shares of Common Stock are reserved for future issuance

in connection with the Company Equity Plans and (v) no shares of Preferred Stock are outstanding. Except as set forth in this Section 4.5 and except for the Shares and Additional Shares to be issued pursuant to this Agreement, there are no (x) shares or other equity interests of the Company or securities of the Company convertible into or exchangeable for shares or other equity interests of the Company, (y) options, warrants, calls, preemptive (or similar) rights, subscriptions, conversion rights, stock appreciation rights, performance units, phantom stock rights, profit participation rights or (z) other rights, agreements, arrangements or commitments of any character relating to the issued or unissued share capital of the Company or obligating the Company to issue, transfer or sell, or cause to be issued, transferred or sold, any shares of share capital, or other equity interests in, the Company or any securities convertible into or exchangeable for such shares or other equity interests of the Company, including any rights, agreements, arrangements or commitments related to any "at the market offering," as defined in the Securities Act, (the items described in clauses (x), (y) and (z), collectively, "***Company Securities***"), and there are no outstanding contractual obligations of the Company or any of its Subsidiaries to repurchase, redeem or otherwise acquire, or prepare and file with the Commission any registration statement to register under the Securities Act with respect to, any such shares of share capital or other equity interests, or to provide funds to, make any investment (in the form of a loan, capital contribution or otherwise) in, return capital to, or make any payment to, any Person. There exist no preemptive (contractual, statutory or otherwise), or other similar rights to purchase securities of the Company.

(b) There are no bonds, debentures, notes or other indebtedness of the Company or any of its Subsidiaries having the right to vote (or convertible into or exercisable for securities having the right to vote) on any matters related to the Company or any of its Subsidiaries, or on which equityholders of the Company or any of its Subsidiaries may vote, issued or outstanding. None of the Company or any of its Subsidiaries is a party to any stockholders' agreement, voting trust agreement or registration rights agreement relating to any equity securities of the Company or any of its Subsidiaries or any other contract relating to disposition, voting or dividends with respect to any Company Securities or any securities of any Subsidiaries of the Company.

(c) All issued and outstanding shares of Common Stock are entitled to one (1) vote per share on each matter properly submitted to the stockholders of the Company for their vote.

4.6. **Subsidiaries**. The Company does not own or control, directly or indirectly, any Person other than the Subsidiaries listed in the SEC Reports. The Company owns, directly or indirectly, all of the capital stock or other equity interests of each Subsidiary listed in the SEC Reports free and clear of any and all Liens, and all the issued and outstanding shares or other equity interest of each such Subsidiary are duly authorized, validly issued, fully paid and non-assessable and were issued free of preemptive (or similar) rights. Except as set forth in the SEC Reports, neither the Company nor any of its Subsidiaries owns, directly or indirectly, any equity interest in any other Person.

4.7. **SEC Documents; Financial Statements**.

(a) Each of Arcturus-Israel and Arcturus-Delaware has filed in a timely manner all reports, schedules, forms, exhibits, statements and other documents that such entity was required to file with the Commission under Sections 13, 14(a) and 15(d) of the Exchange Act or otherwise under the Securities Act or the Exchange Act, since January 1, 2016 (such documents, the "***Applicable SEC Documents***"). As of their respective filing dates (or, if amended prior to the date of this Agreement, when amended), the Applicable SEC Documents complied in all material respects with the requirements of the Exchange Act and the rules and regulations of the Commission promulgated thereunder. None of the Applicable SEC Documents as of their respective dates (and as of the dates filed, mailed or declared effective) contained any untrue statement of material fact or omitted to state a material fact required to be stated therein or necessary to make the statements made therein, in light of the circumstances under which they were made, not misleading. The financial statements of the Company included in the Applicable SEC Documents (the "***Financial Statements***") comply in all material respects with applicable accounting requirements and with the rules and regulations of the Commission with respect thereto. The Financial Statements have been prepared in accordance with GAAP, consistently applied, and fairly present the consolidated financial position, results of operations and cash flows of the Company and its Subsidiaries as at the respective dates thereof and for the respective periods then ended (subject, in the case of unaudited statements, to normal and recurring year-end adjustments, none of which are expected to be material to the Company and its Subsidiaries, taken as a whole). As of the date of this Agreement, there are no unresolved comments in comment letters received from the Commission or its staff. None of the Company's Subsidiaries is subject to the reporting requirements of the Exchange Act.

(b) The Company and its Subsidiaries maintain a system of internal controls over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) sufficient to provide reasonable assurance that (i) transactions are executed in accordance with management's general or specific authorizations; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with GAAP and to maintain asset accountability; (iii) access to assets is permitted only in accordance with management's general or specific authorization; and (iv) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences. The Company's internal controls over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) are effective to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP. Neither the Company nor, to the knowledge of the Company, the Company's independent registered public accounting firm has identified or been made aware of (x) any "significant deficiency" or "material weakness" (each as defined in Rule 13a-15(f) of the Exchange Act) in the system of internal control over financial reporting utilized by the Company and its Subsidiaries that has not been subsequently remediated; or (y) any fraud that involves the Company's management or other employees who have a significant role in the preparation of financial statements or the internal control over financial reporting utilized by the Company and its Subsidiaries, and the Company's principal executive

officer and its principal financial officer have disclosed, based on their evaluation of internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15(d)-15(f)), to the Company's auditors and the audit committee of the Company's board of directors any instances of "significant deficiencies," "material weaknesses" or fraud referred to in clauses (x) and (y). The Company maintains "disclosure controls and procedures" (as such term is defined in Rule 13a-15(e) under the Exchange Act); such disclosure controls and procedures are effective.

(c) There is and has been no failure on the part of the Company and any of the Company's directors or officers, in their capacities as such, to comply with any applicable provision of the Sarbanes-Oxley Act of 2002 and the rules and regulations promulgated in connection therewith, including Section 402 relating to loans and Sections 302 and 906 related to certifications.

4.8. **Material Changes; Undisclosed Events, Liabilities or Developments**. Since December 31, 2018, except as specifically set forth in a subsequent publicly available SEC Report: (a) there has been no Effect that has had or could reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect, (b) the Company has not incurred any liabilities or obligations (contingent or otherwise) other than liabilities not required to be reflected in the Company's financial statements pursuant to GAAP or disclosed in the SEC Reports or liabilities and obligations incurred in the ordinary course of business consistent with past practice since the date of the most recent consolidated balance sheet of the Company and its Subsidiaries included in the SEC Reports publicly available prior to the date hereof, (c) the Company has not altered its method of accounting or the manner in which it keeps its accounting books and records, (d) the Company has not declared or made any dividend or distribution of cash or other property or purchased, redeemed or made any agreements to purchase or redeem any shares of its capital stock, and (e) the Company has not sold, exchanged or otherwise disposed of any material assets or rights. The Company does not have pending before the SEC any request for confidential treatment of information. The Company and its Subsidiaries, individually and on a consolidated basis, are not, as of the date of this Agreement and after giving effect to the transactions contemplated hereby, insolvent.

4.9. **Nasdaq Compliance**. The Common Stock is registered pursuant to Section 12(b) of the Exchange Act and listed on Nasdaq, and the Company has taken no action designed to terminate, or which to its knowledge is likely to have the effect of terminating, the registration of its Common Stock under the Exchange Act or delisting its Common Stock from Nasdaq. The Company is in compliance with applicable Nasdaq continued listing requirements. There are no proceedings pending or, to the Company's knowledge, threatened against the Company relating to the continued listing of the Common Stock on Nasdaq, and the Company has not received any notice of, nor, to the Company's knowledge, is there any reasonable basis for, the delisting of the Common Stock from Nasdaq.

4.10. **Governmental Consents**. No consent, approval, qualification, order, permit or authorization of, or filing with or notification to, any Governmental Authority is required on the part of the Company or, in the case of the Amendment, Arcturus in connection with the Company's or, in the case of the Amendment, Arcturus's valid execution, delivery, or performance of this Agreement, the Registration Rights Agreement or the Amendment, or the consummation of the

transaction contemplated hereby, including the offer, sale or issuance of the Shares and the Additional Shares by the Company, or thereby, other applicable filings with Nasdaq, under the Securities Act or the Exchange Act, in each case, which will be timely filed within the applicable periods therefor.

4.11. **Employees and Employee Matters**. The Company has complied in all material respects with all federal, state and local laws relating to the hiring of employees, consultants and advisors and the employment of labor, including provisions thereof relating to wages, hours, equal opportunity, discrimination, sexual harassment, disability rights or benefits, collective dismissals, plant closures, affirmative action, workers' compensation, severance or other termination-related payments, worker classification, labor relations, occupational safety and health requirements, unemployment insurance, collective bargaining and the payment of social security and other taxes. The Company is not delinquent in material payments to any of its employees for any wages, salaries, commissions, bonuses or other direct compensation for any services performed by them to date or amounts required to be reimbursed to such employees or upon any termination of the employment of any such employees.

4.12. **Material Contracts**. Except as disclosed in the SEC Reports, neither the Company nor any of its assets, properties, businesses or operations is a party to, bound or affected by, or receives benefits under any contract which is a "material contract" (as such term is defined in Item 601(b)(10) of Regulation S-K of the SEC) (a "***Material Contract***"). Except as has not had and could not reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect, (a) each Material Contract is valid and binding on the Company and, to the Company's knowledge, each other party thereto, and in full force and effect, (b) each Material Contract is enforceable against the Company and, to the Company's knowledge, the other parties thereto in accordance with the terms thereof, except as such enforceability may be limited by the Equitable Exceptions, (c) none of the Company, any of its Subsidiaries or, to the Company's knowledge, any other party is in material breach or material violation of, or material default under, any Material Contract and no event has occurred which, with notice or the lapse of time or both, would constitute such a material breach, material violation or material default and (d) neither the Company nor any of its Subsidiaries has received written notice of a claim that it is in material breach or material violation of, or material default under, any Material Contract (whether or not such material default or material violation has been waived). No party to any Material Contract (a) has cancelled or otherwise terminated such Material Contract prior to the expiration of the contract term or (b) to the knowledge of the Company, has threatened to terminate the applicable Material Contract.

4.13. **Litigation**. There is no material Action pending or, to the Company's knowledge, currently threatened against the Company, any of its Subsidiaries, any of their respective directors, officers or employees or any property, right or asset of the Company or any of its Subsidiaries. None of the Company, any of its Subsidiaries, or any property, right or asset of the Company or any of its Subsidiaries is a party to, or subject to the provisions of, any order writ, injunction, judgment, award, ruling or decree of, or settlement agreement with, any Governmental Authority. Neither the Company nor any of its Subsidiaries, nor, to the Company's knowledge, any of their respective directors or officers, is or has been the subject of any Action involving a claim of violation of or liability under securities Laws or a claim of breach of fiduciary duty. There has not been, and, to the Company's knowledge, there is not pending or contemplated, any investigation by the Commission involving the Company, any of its Subsidiaries or, to the Company's

knowledge, any of their respective current or former directors or officers. The Commission has not issued any stop order or other order suspending the effectiveness of any registration statement filed by the Company or any of its Subsidiaries under the Exchange Act or the Securities Act.

4.14. **Taxes**.

(a) Except as has not had and could not reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect, (i) all U.S. federal, state and local and Israeli and other non-U.S. tax returns, reports and declarations of the Company and any Subsidiary required by Law to be filed have been duly filed and (ii) all taxes and other fees due and owing as required by Law have been paid. There is no tax Lien, whether imposed by any federal, state, county or local or Israeli or other non-U.S. taxing authority, outstanding against the assets, properties or business of the Company or any of its Subsidiaries.

(b) No U.S. federal, state, local or Israeli or other non-U.S. tax audits or administrative or judicial tax proceedings are pending or being conducted with respect to the Company or any of its Subsidiaries. Neither the Company nor any of its Subsidiaries has received from any U.S. federal state, local or Israeli or other non-U.S. taxing authorities any (i) notice indicating an intent to open and audit or other review, (ii) request for information related to tax matters, or (iii) notice of deficiency or proposed adjustment for any amount of tax proposed, asserted, or assessed by any taxing authority against the Company or any of its Subsidiaries.

(c) No claim has ever been made by any taxing authority in a jurisdiction where the Company or any of its Subsidiaries does not file tax returns that the Company or any of its Subsidiaries is or may be subject to taxation in that jurisdiction.

(d) Neither the Company nor any of its Subsidiaries has waived any stature of limitation in respect of taxes or agreed to any extension of time with respect to a tax assessment or deficiency.

(e) The Company and each of its Subsidiaries have withheld and paid all taxes required to have been withheld and paid in connection with any amounts paid or owing to any employee, independent contractor, creditor, stockholder, or other third party.

(f) Neither the Company nor any of its Subsidiaries will be required to include any items of income in, or exclude any items of deduction from, taxable income for any tax period after the Closing Date as a result of any (i) change in method of accounting for a taxable period ending on or prior to the Closing Date, (ii) "closing agreement" as described in Code Section 7121 (or any corresponding or similar provision of state, local, or non-U.S. income tax Law) executed prior to the Closing, (iii) intercompany transaction described in the Treasury Regulations promulgated under Code Section 1502 (or any corresponding or similar provision of state, local, or non-U.S. Law) occurring prior to the Closing Date, (iv) installment sale or open transaction disposition made prior to the Closing, (v) prepaid amount received prior to the Closing or (vi) election under Code Section 108(i).

(g) At all times since November 15, 2017, the Company has been treated as a U.S. corporation for U.S. federal income tax purposes pursuant to Code Section 7874.

(h) Neither the Company nor any of its Subsidiaries has been a party to any "reportable transaction" as defined in Code Section 6707A(c)(1).

4.15. **Affiliate Transactions**. No employee, officer, director or 5% or greater shareholder of the Company or member of his or her immediate family (each a "***Covered Person***") is currently indebted to the Company, nor is the Company indebted (or committed to make loans or extend or guarantee credit) to any Covered Person. Except as disclosed in the SEC Reports, no Covered Person has any direct or indirect ownership interest in any firm or corporation with which the Company is affiliated or with which the Company has a business relationship, or any firm or corporation that competes with the Company (except for ownership of stock not to exceed 1% of the outstanding capital stock of any publicly traded company that may compete with the Company).

4.16. **Title to Assets**. Except as set forth in the SEC Reports, the Company and its Subsidiaries have good and marketable title to all real property and personal property owned by the Company or its Subsidiaries that is material to the business of the Company and its Subsidiaries, taken as a whole, in each case free and clear of all Liens, except for Liens that do not materially affect the value of such property and do not materially interfere with the use made and proposed to be made of such property by the Company and its Subsidiaries and Liens for the payment of federal, state or other taxes, the payment of which is neither delinquent nor subject to penalties. Any real property and facilities held under lease by the Company or any of its Subsidiaries are held by them under valid, subsisting and enforceable leases with which the Company and its Subsidiaries are in compliance.

4.17. **Foreign Corrupt Practices**. None of the Company, its Subsidiaries or any director, officer, employee or agent of the Company or any of its Subsidiaries or, to the knowledge of the Company, any other Person acting on behalf of the Company or any of its Subsidiaries has: (a) directly or indirectly, used any funds for unlawful contributions, gifts, entertainment or other unlawful expenses related to foreign or domestic political activity, (b) made any unlawful payment to foreign or domestic government officials or employees or to any foreign or domestic political parties or campaigns from corporate funds, (c) failed to disclose fully any contribution made by the Company or any of its Subsidiaries (or made by any Person acting on its behalf of which the Company is aware) which is in violation of Law or (d) violated any provision of the Foreign Corrupt Practices Act of 1977, as amended, or any applicable anti-bribery Law.

4.18. **Office of Foreign Assets Control**. None of the Company, its Subsidiaries or any director, officer, employee or agent of the Company or any of its Subsidiaries or, to the knowledge of the Company, any other Person acting on behalf of the Company or any of its Subsidiaries, (a) is currently subject to any sanctions administered by the Office of Foreign Assets Control of the U.S. Treasury Department ("***Sanctions***") or (ii) will, directly or indirectly, use the proceeds of this offering, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other Person in any manner that will result in a violation of any Sanctions by, or could result in the imposition of Sanctions against, any Person, or (b) is a Person that is, or is 50% or more owned or otherwise controlled by a Person that is: (i) the subject of any Sanctions;

or (ii) located, organized or resident in a country or territory that is, or whose government is, the subject of Sanctions.

4.19. **Money Laundering**. The operations of the Company and its Subsidiaries are and have been conducted at all times in compliance with applicable financial record-keeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, applicable money laundering statutes and applicable rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any Governmental Authority (collectively, the "***Money Laundering Laws***"), and no Action involving the Company or any of its Subsidiaries with respect to the Money Laundering Laws is pending or, to the knowledge of the Company, threatened.

4.20. **Offering Exemption**. Assuming the accuracy of the representations made by the Investor in Section 5.2, the offer and issuance by the Company of the Shares and the Additional Shares is exempt from registration under the Securities Act and all applicable state and foreign registration or qualification requirements.

4.21. **Compliance with Rule 506**. None of the Company, any of its predecessors, any affiliated issuer, any director, executive officer, other officer of the Company participating in the offering contemplated hereby, any beneficial owner of 20% or more of the Company's outstanding voting equity securities, calculated on the basis of voting power, any promoter (as that term is defined in Rule 405 under the Securities Act) connected with the Company in any capacity at the time of sale nor any other Person specified in Rule 506(d)(1) under the Securities Act is disqualified from relying on Rule 506 of Regulation D under the Securities Act ("***Rule 506***") for any of the reasons stated in Rule 506(d) in connection with the issuance and sale of the Shares and the Additional Shares to the Investor pursuant to this Agreement. The Company has exercised reasonable care, including conducting a factual inquiry that is appropriate in light of the circumstances, into whether any such disqualification under Rule 506(d) exists, but has assumed the accuracy of the Investor's representations and warranties.

4.22. **No General Solicitation**. None of the Company, any of its Affiliates, or any Person acting on its or their behalf, has engaged in any form of general solicitation or general advertising (within the meaning of Regulation D promulgated under the Securities Act) in connection with the offer or sale of the Shares or Additional Shares.

4.23. **No Integrated Offering**. None of the Company, any of its Affiliates, or any Person acting on its or their behalf has, directly or indirectly, made any offers or sales of any security or solicited any offers to buy, or otherwise negotiated in respect of, any security, under circumstances that would adversely affect reliance by the Company on Section 4(a)(2) of the Securities Act or require registration of any of the Shares or Additional Shares under the Securities Act or cause this offering of the Shares or Additional Shares to be integrated with other offerings by the Company (including those contemplated by Section 3.5) for purposes of the Securities Act or any applicable stockholder approval provisions, including under the rules and regulations of Nasdaq.

4.24. **Intellectual Property; Trials**.

(a) The Company owns or possesses all (i) patents, patent applications, trademarks, trademark registrations, service marks, service mark registrations, Internet domain name registrations, copyrights, copyright registrations, licenses and trade secret rights (collectively, "***Intellectual Property Rights***") and (ii) inventions, software, works of authorships, trademarks, service marks, trade names, databases, formulae, know how, Internet domain names and other intellectual property (including trade secrets and other unpatented and/or unpatentable proprietary confidential information, systems, or procedures) (collectively, "***Intellectual Property Assets***") necessary to conduct its business as currently conducted, and as proposed to be conducted and described in the Applicable SEC Documents. The Company has not received any opinion from its legal counsel concluding that any activities of its business infringes, misappropriates, or otherwise violates, valid and enforceable Intellectual Property Rights of any other person, and has not received written notice of any challenge, which is, to its knowledge, still pending, by any other Person to the rights of the Company or its Subsidiaries with respect to any Intellectual Property Rights or Intellectual Property Assets owned or used by the Company and its Subsidiaries. The Company and its Subsidiaries have complied in all material respects with, and are not in breach of, nor have they received any asserted or threatened written claim of breach of any intellectual property licenses for the use of the Intellectual Property Rights, and the Company has no knowledge of any breach or intended breach by any Person of any such intellectual property licenses. No claim has been made in writing or is pending against the Company or any of its Subsidiaries alleging the infringement by the Company or any of its Subsidiaries of any patent, trademark, service mark, trade name, copyright, trade secret, license in or other intellectual property right or franchise right of any Person.

(b) The studies, tests and preclinical or clinical trials conducted by or on behalf of the Company or any of its Subsidiaries (the "***Company Studies and Trials***") were and, if still pending, are being conducted in all material respects in accordance with experimental protocols, procedures and controls pursuant to, where applicable, accepted professional scientific standards; the descriptions of the results of the Company Studies and Trials contained in the Applicable SEC Documents are accurate in all material respects. The Company has not received any notices or correspondence from the United States Food and Drug Administration or any Governmental Authority exercising comparable authority requiring the termination, suspension or material modification of any Company Studies and Trials, except for any such termination, suspension or material modification that has not had and could not reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect and, to the Company's knowledge, there are no reasonable grounds for the same.

4.25. **Insurance**. The Company and each of its Subsidiaries are insured by insurers of recognized financial responsibility against such losses and risks and in such amounts as are reasonable and customary in the business in which it is engaged. All policies of insurance and fidelity or surety bonds insuring the Company and each of its Subsidiaries or their respective businesses, assets, employees, officers and directors are in full force and effect. The Company has no reason to believe that it and each of its Subsidiaries will not be able to renew its existing

insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business at a cost that would not be significant.

4.26. **Compliance with Laws; Permits**. (a) Except as has not had and could not reasonably be excepted to have, individually or in the aggregate, a Material Adverse Effect, (i) the Company and its Subsidiaries, since January 1, 2017, have conducted and are conducting their businesses in compliance with all Laws (including all Environmental Laws) applicable to the Company, any of its Subsidiaries or any of their assets, (ii) neither the Company nor any of its Subsidiaries has received any notification or communication from any Governmental Authority of any alleged, potential or actual violation by the Company or any of its Subsidiaries of any Law and (iii) the Redomiciliation complied with all applicable Laws. The Company is not a "potentially responsible party" under any Environmental Laws.

(b) The Company and its board of directors have taken all necessary action, if any, in order to render inapplicable any control share acquisition, business combination, poison pill (including any distribution under a rights agreement) or other similar anti-takeover provision under the Company's Organizational Documents or the Laws of its state of incorporation that is or could become applicable to the Investor as a result of the Investor and the Company performing their obligations or exercising their rights under this Agreement.

(c) The Company and each of its Subsidiaries possess all licenses, certificates, consents, approvals, permits and other authorizations issued by all applicable authorities necessary to conduct their respective businesses (collectively, "***Permits***"), and neither the Company nor any of its Subsidiaries is or has been in conflict with, or in default, breach or violation of, any Permit or has received any notice of proceedings relating to the revocation or modification of any such Permit which, if the subject of an unfavorable decision, ruling or finding, could reasonably be expected to have, individually or in the aggregate, a Material Adverse Effect.

4.27. **Approval of Transaction**. The Company's board of directors has approved the transactions contemplated by this Agreement, including the issuance of the Shares and the Additional Shares to the Investor (including for purposes of Section 203 of the Delaware General Corporation Law and Rule 16(b)(3) of the Exchange Act).

4.28. **Investment Company**. The Company is not and, after giving effect to the offering and sale of the Shares and Additional Shares, will not be an "investment company" as defined in the Investment Company Act of 1940, as amended.

4.29. **Disclosure**. The Company understands and confirms that the Investor will rely on the foregoing representations in effecting transactions in securities of the Company. To the knowledge of the executive officers of the Company, all due diligence materials regarding the Company and its Subsidiaries, their businesses and the transactions contemplated hereby, furnished by or on behalf of the Company to the Investor upon its request are, when taken together with the SEC Reports, true and correct in all material respects and do not contain any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements made therein, in light of the circumstances under which they were made, not misleading.

4.30. **Brokers or Finders**. The Company has not retained any brokers, consultants, finders, investment bankers or advisors in connection with this Agreement or the transactions contemplated hereby, and has no agreements to pay any commission or compensation in the nature of a finder's, broker's or other fee arising out of this Agreement or the transactions contemplated hereby.

5. **Representations and Warranties of the Investor**. The Investor hereby represents and warrants, as of the date hereof and as of the Closing Date, to the Company as follows:

5.1. **Authorization; Enforceability**. The Investor has all requisite corporate power and authority, and has taken all requisite corporate action, to execute and deliver this Agreement, the Registration Rights Agreement and the Amendment, to consummate the transactions contemplated hereby and thereby and to perform all of its obligations hereunder and thereunder. Upon the execution and delivery of this Agreement and the Registration Rights Agreement by the Investor, each of this Agreement and the Registration Rights Agreement shall constitute a valid and binding obligation of the Investor, enforceable in accordance with its terms, except as may be limited by the Equitable Exceptions.

5.2. **Investment Representations**.

(a) The Investor has such knowledge and experience in financial and business matters that the Investor is capable of evaluating the merits and risks of the Investor's prospective investment in the Company and has the ability to bear the economic risks of the investment contemplated hereby.

(b) Investor is acquiring the Shares and the Additional Shares for investment for the Investor's own account and not with the present view to, or for present resale in connection with, any distribution thereof in violation of the Securities Act (without prejudice, however, to the Investor's rights to sell or otherwise distribute the Shares and Additional Shares in compliance with this Agreement). The Investor understands that the Shares and the Additional Shares have not been registered under the Securities Act by reason of a specific exemption from the registration provisions of the Securities Act. The Investor further represents that it does not, as of the date of this Agreement, have any contract, undertaking, agreement or arrangement with any Person to sell, transfer or grant participation to any third Person with respect to any of the Shares or the Additional Shares.

(c) The Investor acknowledges that the Shares and the Additional Shares may only be sold if subsequently registered under the Securities Act or an exemption from such registration is available. The Investor is aware of the provisions of Rule 144 that permit limited resale of shares purchased in a private placement subject to the satisfaction of certain conditions.

(d) The Investor has received and reviewed information about the Company and has had an opportunity to discuss the Company's business, management and financial affairs with its management and to review the Company's facilities. The Investor has had an opportunity to ask questions of and receive answers from the Company, or any

Person or Persons acting on behalf of the Company, concerning the terms and conditions of an investment in the Shares and the Additional Shares.

(e) The Investor acknowledges that it is an "accredited investor" as defined in Rule 501(a) of Regulation D of the Securities Act.

(f) The Investor was not induced to participate in the offer and sale of the Shares and the Additional Shares by the filing of any registration statement in connection with any public offering of the Company's securities (other than pursuant to the Registration Rights Agreement).

5.3. **Brokers**. There are no brokers, finders or financial advisory fees or commissions that will be payable by the Investor in respect of the transactions contemplated by this Agreement.

5.4. **Legends**. The Investor understands that, until such time as the Shares or the Additional Shares have been sold pursuant to the Registration Statement (as such term is defined in the Registration Rights Agreement) or the Shares or the Additional Shares may be sold pursuant to Rule 144 without any restriction as to the number of securities as of a particular date that can then be immediately sold, the book entry notations evidencing the Shares and the Additional Shares may bear one or more legends in substantially the following form and substance:

"THE SECURITIES REPRESENTED HEREBY HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), OR UNDER THE SECURITIES LAWS OF CERTAIN STATES. THESE SECURITIES ARE SUBJECT TO RESTRICTIONS ON TRANSFERABILITY AND RESALE AND MAY NOT BE TRANSFERRED OR RESOLD EXCEPT (1) AS PERMITTED UNDER THE ACT AND ANY APPLICABLE STATE SECURITIES LAWS, PURSUANT TO REGISTRATION OR EXEMPTION THEREFROM, (2) UNLESS THE COMPANY HAS RECEIVED AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY AND ITS COUNSEL THAT SUCH REGISTRATION IS NOT REQUIRED OR (3) UNLESS SOLD PURSUANT TO RULE 144 OF THE ACT OR OTHER EXEMPTION FROM REGISTRATION."

6. Covenants.

6.1. **Standstill**. Subject to Section 6.3, the Investor hereby agrees that, without the prior approval of the Company, the Investor shall not, and shall not permit any controlled Affiliate to, (except as contemplated by this Agreement or as approved or invited by the Company):

(a) acting alone or with others, acquire, offer to acquire, or agree to acquire, directly or indirectly, by purchase, merger, business combination or in any other manner, any voting equity securities of the Company if, after such acquisition, the Investor, together with its controlled Affiliates, would own more than the Threshold; provided that any investment by the Investor or an Affiliate of the Investor, or any of their respective pension or employee benefit plans, in third-party mutual funds or other similar passive investment vehicles that hold interests in securities of the Company or any of its Affiliates shall not be taken into account for the purpose of this subparagraph (a) or otherwise prohibited by this Section 6.1 (provided that, neither the Investor nor any of its controlled Affiliates shall request or direct that the trustee

or other administrator of any such plans, funds or other similar passive investment vehicles acquire equity securities of the Company);

(b) engage in any "solicitation" of "proxies" (as such terms are used in the rules promulgated by the Commission) to vote any voting equity securities of the Company, or seek to advise or influence any Person with respect to the voting of any voting equity securities of the Company (other than in connection with the election of the Investor Designee);

(c) form, join or in any way participate in a "group" as defined in Section 13(d)(3) (a "***13D Group***") of the Exchange Act, in connection with any of the foregoing clauses (a) and (b) (other than a 13D Group that includes only the Investor and its Affiliates or that relates to the Investor Designee);

(d) publicly disclose any intention, plan or arrangement inconsistent with the foregoing clauses (a) through (c); or

(e) enter into any agreement or any arrangement with any other Person in connection with intentionally facilitating any transaction that is restricted by clauses (a) through (c);

provided that, notwithstanding anything in this Agreement to the contrary, (x) the Investor and its Affiliates shall not be prohibited or restricted from making (i) any confidential offers or proposals to the Company's board of directors or engaging in negotiation or discussions with the Company with respect thereto or (ii) any confidential request for the Company or its board of directors to waive, amend or provide a release of any provision of this Section 6.1 (whether or not in connection with such offer or proposal), (y) the Investor and its Affiliates may vote their shares of Common Stock in any manner they wish and (z) the provisions of this Section 6.1 shall not, and are not intended to, (i) restrict the manner in which any Investor Designee may (A) vote on any matter submitted to the Company's board of directors, (B) participate in deliberations or discussions of the Company's board of directors (including making suggestions or raising issues to the Company's board of directors) in his or her capacity as a member of the Company's board of directors, or (C) take actions required by his or her exercise of legal duties and obligations as a member of the Company's board of directors or refrain from taking any action prohibited by his or her legal duties and obligations as a member of the Company's board of directors, (ii) prohibit or restrict the Investor or its Affiliates from responding to any inquiries from any stockholders of the Company as to such Person's intention with respect to the voting or the tendering of its Common Stock, (iii) restrict the Investor or its Affiliates from taking any action they deem necessary to cause the Investor Designee to be elected to the Company's board of directors or any committee thereof or causing or effecting the issuance and acquisition of the Additional Shares, (iv) prohibit the Investor or its Affiliates from acquiring Company Securities issued by way of a Stock Event or which are issued to its directors, (v) prohibit the Investor or its Affiliates from selling their shares of Common Stock or (vi) prohibit the Investor or its Affiliates from complying with applicable Law.

6.2. **Transfer Restrictions**. Subject to Section 6.3, the Investor shall not, directly or indirectly, sell, transfer, pledge, contract to sell, sell any option or contract to purchase, purchase

any option or contract to sell, grant any option, right or warrant to purchase, transfer the economic risk of ownership of, or otherwise dispose of (each, a "***Transfer***") any of the Shares or Additional Shares, except:

(a) to the Company;

(b) in response to a tender offer or exchange offer subject to Regulation 14D or Rule 13e-3 of the rules promulgated under the Exchange Act by the Commission, for cash, securities or other consideration;

(c) in connection with a Change of Control of the Company;

(d) to comply with the terms of this Agreement; or

(e) to an Affiliate of Investor in one or more transactions, so long as prior to or concurrent with any such Transfer such Affiliate agrees in writing to be bound by the terms of this Agreement;

provided that, for the avoidance of doubt, nothing in this Section 6.2 will restrict any Transfer of Shares or Additional Shares that may occur (or be deemed to occur) in connection with a Change of Control of the Investor (replacing references to "Company" with "Investor" in the definition of "Change of Control").

6.3. **Termination of Standstill and Transfer Restrictions**.

(a) The restrictions set forth in Section 6.1 shall terminate upon the earliest to occur of the following:

(i) (v) the merger, consolidation or other business combination or transaction to which the Company or any of its Subsidiaries is a party (other than a transaction solely between the Company and one or more of its wholly-owned Subsidiaries); (w) an acquisition by any Person or 13D Group (other than a 13D Group of which Investor or any of its Affiliates is a member) of direct or indirect beneficial ownership of voting securities (or securities convertible into or exercisable or exchangeable for such voting securities) of the Company or any of its Subsidiaries representing 50% or more of the total number of votes which may be cast in the election of members of the Company's board of directors if all securities entitled to vote in the election of such directors are present and voted ("***Total Voting Power***") or 50% or more of the total number of voting securities (or securities convertible into or exercisable or exchangeable for such voting securities) of any of the Company's Subsidiaries; (x) a sale, lease, exchange, contribution or other transfer (in one transaction or a series of related transactions) of all or substantially all of the assets of the Company or its Subsidiaries; (y) a liquidation or dissolution of the Company or (z) individuals who constitute Continuing Directors ceasing for any reason to constitute at least a majority of the Company's board of directors (clauses (v) through (z), collectively, a "***Change of Control***");

(ii) the date on which the Common Stock ceases to be registered pursuant to Section 12 of the Exchange Act;

(iii) if, at any time that the Investor is entitled to appoint an Investor Designee, (A) such Investor Designee is not elected or appointed to the Company's board of directors (or any committee thereof that the Investor Designee is eligible to be a member of pursuant to this Agreement) within five (5) Business Days after such election or appointment is required under this Agreement, (B) such Investor Designee is removed from the Company's board of directors or any such committee (other than at the direction of the Investor) or (C) the Company otherwise breaches Section 6.7 in any material respect; or

(iv) the two (2) year anniversary of the Closing Date.

(b) The restrictions set forth in Section 6.2 shall terminate upon the earliest to occur of the following:

(i) a Change of Control;

(ii) the date on which the Common Stock ceases to be registered pursuant to Section 12 of the Exchange Act;

(iii) the termination of the Collaboration Agreement;

(iv) if, at any time that the Investor is entitled to appoint an Investor Designee, (A) such Investor Designee is not elected or appointed to the Company's board of directors (or any committee thereof that the Investor Designee is eligible to be a member of pursuant to this Agreement) within five (5) Business Days after such election or appointment is required under this Agreement, (B) such Investor Designee is removed from the Company's board of directors or any such committee (other than at the direction of the Investor) or (C) the Company otherwise breaches Section 6.7 in any material respect;

(v) the date on which the Investor beneficially owns less than eight percent (8%) of the Total Voting Power; or

(vi) with respect to the Shares purchased at the Closing, the earlier of (a) the second anniversary of the Closing Date or (b) the six-month anniversary of the Additional Closing Date, and, with respect to any Additional Shares, the six-month anniversary of the Additional Closing Date on which the Investor purchased such Additional Shares.

(c) The restrictions set forth in Section 6.1 and the restrictions set forth in Section 6.2 shall terminate and shall not apply to or otherwise restrict the Investor's or its Affiliates' actions in respect of the Company Securities if a Significant Event has occurred (whether by way of purchase, merger, consolidation, tender offer, exchange offer or otherwise). For purposes of this Section 6.3(c) a "***Significant Event***" shall mean any of the following not involving a violation of Section 6.1: (i) the public announcement of a proposal to acquire (and such proposal has not been publicly rejected by the Company's board of directors within two Business Days from the date of such public announcement), or the acquisition, by any Person or 13D Group of beneficial ownership of voting securities of the Company or any of its Subsidiaries representing (A) 20% or more of the then outstanding Common Stock or Total Voting Power, (B) securities convertible into or exercisable or exchangeable for 20% or more

of the outstanding Common Stock or Total Voting Power, (C) any options, warrants or other rights to acquire 20% or more of the outstanding Common Stock or Total Voting Power, (D) 20% or more of any securities of any Subsidiary of the Company or, (E) assets or groups of assets having a book value in excess of 20% of the total book value of the assets of the Company and its Subsidiaries, taken as a whole (each, a "***Controlling Stake***"); (ii) the commencement or public announcement of an intention to commence, by any Person or 13D Group, of a tender or exchange offer, to acquire voting securities of the Company which has not been publicly rejected (within two Business Days from the date of such commencement or public announcement) by the Company's board of directors, and which, if successful, would result in such Person or 13D Group owning, when combined with any other voting securities of the Company owned by such Person or 13D Group, a Controlling Stake; (iii) the entry into by the Company, or the public announcement by the Company of a determination to explore, enter into or commence or continue any discussions relating to, any merger, consolidation, sale or other business combination transaction, or an agreement therefor, pursuant to which the outstanding shares of capital stock of the Company would be converted into cash, other consideration or securities of another Person or 13D Group or 50% or more of the then outstanding shares of capital stock of the Company would be owned by Persons other than the then current holders of shares of capital stock of the Company, which would result in all or a substantial portion of the Company's or any of its Subsidiaries' assets being sold to any person or 13D Group or which could otherwise lead to a Change of Control; (iv) the submission of any bona fide offer by any Third Party for a Controlling Stake or Change of Control (and the Company's board of directors permits the Company to negotiate in respect of such Third Party offer), prompt notice of which shall be provided to the Investor (such notice not to be later than three (3) Business Days after such submission); or (v) the public announcement by the Company that it is reviewing or is engaged in a process related to its strategic alternatives.

6.4. **Certain Offerings**. At any time prior to termination of the restrictions set forth in both Section 6.1 (unless such restrictions terminate pursuant to Section 6.3(a)(ii) or Section 6.3(a)(iii), in which case such rights shall continue until Section 6.1 would otherwise have been terminated) and Section 6.2 (unless such restrictions terminate pursuant to Section 6.3(b)(ii), Section 6.3(b)(iii) or Section 6.3(b)(iv) , in which case such rights shall continue until Section 6.2 would otherwise have been terminated) if the Company proposes to issue additional shares of Common Stock or any other Company Securities (collectively, the "***Offered Securities***") in a (a) broadly marketed, underwritten, public offering of Offered Securities registered under the Securities Act other than a Permitted Issuance, or (b) private placement or registered offering other than a public offering described in clause (a) or a Permitted Issuance, the Company shall use its best efforts to provide the Investor the opportunity to purchase the Offered Securities (up to an amount of Offered Securities that results in beneficial ownership by the Investor and its Affiliates of the same percentage of the issued and outstanding shares of Common Stock (on a fully diluted basis) immediately after giving effect to such purchase that the Investor owned prior to such offering) on the same terms as the other investors in such offering.

6.5. **Indemnification of the Investor**.

(a) Subject to the provisions of this Section 6.5, the Company shall indemnify and hold the Investor, its Affiliates and their respective directors, officers, shareholders, members, partners, employees, agents, successors, assigns and each Person who controls the Investor (within the meaning of Section 15 of the Securities Act and Section 20 of the Exchange Act), and the directors, officers, shareholders, agents, members, partners or employees of such controlling Persons and its Affiliates (each, an "***Investor Party***") harmless for, from and against any and all losses, liabilities, obligations, claims, contingencies, damages, costs and expenses, including all judgments, interest, awards, penalties, amounts paid in settlements, court costs and reasonable attorneys' and consultant's fees and costs of investigation (collectively, "***Losses***") that any such Investor Party may suffer or incur as a result of, or arising out of, the Company's breach of its representations, warranties, covenants or obligations under this Agreement (unless such Loss is solely due to the breach of the Investor's representation set forth in Section 5.2), including, in the case of an Additional Closing, in respect of the certifications made on the Additional Closing Certificate as well as any Losses such Investor Party may suffer or incur as a result of, or arising out of, the Company's breach of its representations, warranties, covenants or obligations under this Agreement that were made on the Closing Date as such Losses relate to the Additional Shares. If any Action shall be brought against any Investor Party in respect of which indemnity may be sought pursuant to this Agreement, such Investor Party shall reasonably promptly notify the Company in writing; provided that the failure to so notify the Company shall not affect the Investor Party's right to indemnification except to the extent the Company is materially prejudiced thereby.

(b) In no event will the Company's liability under this Section 6.5 exceed an aggregate of $10,000,000 in connection with any claim based on a breach of any representations and warranties contained in this Agreement; provided that, notwithstanding the foregoing, with respect to any claim based on a breach of any Company Fundamental Representations, in no event will the Company's liability under this Section 6.5 exceed the purchase price for Shares and Additional Shares paid by the Investor.

6.6. **Listing of Common Stock**. The Company hereby agrees to use its best efforts to (a) maintain the listing and trading of the Common Stock on Nasdaq, and (b) comply in all respects with the Company's reporting, filing and other obligations under the bylaws or rules of Nasdaq.

6.7. **Board Nomination Right**.

(a) Until the later of (x) the first anniversary of the Closing Date or (y) the date on which the Investor beneficially owns less than eight percent (8.0%) of the Total Voting Power (excluding any derivative securities exercisable for the Company's capital stock which have not been exercised), (i) at each annual meeting of the stockholders of the Company or at any meeting of the stockholders of the Company at which members of the board of directors are to be elected, or whenever such action is to be taken by written consent for such purposes, the Company agrees to nominate for election one individual designated by the Investor who shall be reasonably acceptable to the Company (an "***Investor Designee***"), and (ii) the Investor shall have the right to

appoint the chief executive officer of the Investor as a non-voting observer to the Company's board of directors (the "***Investor Observer***"). The Investor's initial Investor Designee under this Agreement shall be Karah Parschauer (the "***Initial Designee***"). On or prior to the Closing Date, the Company shall take all actions necessary to cause the appointment to the Company's board of directors of the Initial Designee effective as of the Closing Date, and thereafter, for so long as the Investor's board nomination right under this Section 6.7 continues, the Company will use its best efforts to cause the election and reelection of such individual to the Company's board of directors for so long as he or she is an Investor Designee (including recommending that the Company's stockholders vote in favor of the election of such an individual, soliciting proxies and contesting any proxy contest and otherwise supporting him for election in a manner no less rigorous and favorable than the manner in which the Company supports its other nominees); provided that if the Investor determines to designate a different individual ("***Replacement Designee***") as its Investor Designee, such obligation shall instead apply to the Replacement Designee. If the Investor Designee vacates the board of directors, the Company shall take all actions necessary to cause the appointment to its board of directors of a Replacement Designee nominated by the Investor to fill the vacancy and thereafter the Company will use its best efforts to cause the election of such an individual to the Company's board of directors, subject to the same conditions and limitations as set forth in the foregoing sentence. The Investor Designee shall be entitled to the same level of directors' and officers' indemnity insurance coverage and indemnity and exculpation protection (including under any indemnification agreement) as the other members of the Company's board of directors. The Company shall enter into a customary indemnification agreement for the benefit of the Investor Designee and the Investor Observer. For so long as an Investor Designee serves on the Company's board of directors, the Company shall maintain in place directors' and officers' indemnity insurance coverage in an amount deemed appropriate by the Company's board of directors. The Investor Designee and the Investor Observer will be required to enter into a customary non-disclosure agreement that each director of the Company is required to enter into as of the date of this Agreement, on terms and conditions reasonably acceptable to the Investor; provided that, for the avoidance of doubt, such non-disclosure agreement shall not impose any other restrictive covenants and shall not restrict the Investor Designee from disclosing information to the Investor or the Investor's ability to use such information in connection with transactions involving or relating to the Company.

(b) If the Investor Designee included in the slate of nominees recommended by the Company's board of directors for election at a meeting of the stockholders of the Company is not elected to be a director at such meeting, the Company shall promptly increase the size of its board of directors and take such other action as is necessary to appoint the Investor Designee to the Company's board of directors.

(c) For so long as the Investor is entitled to designate at least one Investor Designee for election to the Company's board of directors under this Agreement, each committee of the Company's board of directors shall include the Investor Designee other than any *bona fide* special committee solely formed to evaluate any existing or

contemplated change in control transaction (a "***Special Committee***"); provided, however, that if the Investor Designee is not eligible for membership on any given committee of the Company's board of directors (other than a Special Committee) under then applicable listing and corporate governance standards of Nasdaq or any other applicable Law, then such committee shall include the Investor Designee only when so permitted by the listing and corporate governance standards of Nasdaq and any other applicable Law; provided, further, that the Company shall exercise reasonable authority under applicable Law to permit the inclusion of the Investor Designee on such committee, including by causing an increase in the number of directors on such committee. Subject to the foregoing, the Company shall take appropriate action, effective as of the commencement of business on the first business day immediately after the Closing Date, to allow for the appointment of the Initial Designee to the committees of its board of directors.

(d) The Investor Observer shall be entitled to attend all meetings of the Company's board of directors and any committees thereof and to receive copies of all notices, minutes, consents, and other materials provided to the members of the Company's board of directors (or such committees) at the same time and in the same manner as provided to the Company's board of directors (or such committees).

(e) Notwithstanding the foregoing clauses (c) and (d) of this Section 6.7, the Company reserves the right to withhold any information and to exclude the Investor Designee and the Investor Observer from any portion of a board or committee meeting, if (i) such information or portion of such meeting relates to (x) the Collaboration Agreement or any other agreements between the Company and the Investor, (y) any strategic discussions between the Company and the Investor or (z) any Action between the Company and the Investor or (ii) such access to a board or committee meeting, or access to such information, would, based on advice of outside counsel to the Company, adversely affect the attorney-client privilege of the Company's board of directors; provided that such clause (ii) shall only be applicable to the Investor Designee in connection with any pending Action between the Company and the Investor. In addition, the Investor Observer may be excluded from any meeting of the audit, nomination and compensation committees for any reason at the discretion of the respective committee.

(f) **Corporate Opportunity**. The Company renounces any interest or expectancy of the Company in, or in being offered an opportunity to participate in, any matter, transaction or interest that is presented to, or acquired, created or developed by, or which otherwise comes into the possession of (a) the Investor Designee or the Investor Observer or (b) the Investor or its Affiliates (collectively, "***Affiliated Persons***") and waives any claim against each Affiliated Person arising from the fact that such Affiliated Person (i) pursues or acquires any such corporate opportunity for its own account or the account of any Affiliate or other person, (ii) directs, recommends, sells, assigns or otherwise transfers such corporate opportunity to another person or (iii) does not communicate information regarding such corporate opportunity to the Company; provided, that, in each such case, that any corporate opportunity which is

expressly offered to an Affiliated Person in his or her capacity as a member of the Company's board of directors shall belong to the Company.

6.8. **Conduct of Business**.

(a) The Company covenants and agrees that, between the date of this Agreement and the Closing, except with the prior written consent of Investor, the businesses of the Company and its Subsidiaries shall be conducted only in, and the Company and its Subsidiaries shall not take any action except in, the ordinary course of business and in a manner consistent with past practice, and the Company and each of its Subsidiaries shall use their reasonable best efforts to (A) preserve substantially intact their existing assets, (B) preserve substantially intact their business organization, (C) keep available the services of their current officers and key employees, and (D) comply in all material respects with applicable Law.

(b) The Company covenants and agrees that, between the date of this Agreement and the six (6)-month anniversary of the Closing, except with the prior written consent of Investor, it will not, directly or indirectly, declare, set aside or pay any dividend or make any other distribution or payment (whether in cash, stock or property or any combination thereof) in respect of any Company Securities, or establish a record date for any of the foregoing.

6.9. **Post-Closing Restrictions**. The Company shall not, directly or indirectly, take any action or omit to take any action that would (i) conflict with the terms of this Agreement or otherwise effect any rights or obligations of the parties hereunder (including the Investor's right to acquire up to the Threshold) or (ii) disproportionately affect the Investor or its Affiliates (including their voting rights), as compared to any other equityholder of the Company.

6.10. **Form D; Blue Sky Filings**. The Company agrees to timely file a Form D with respect to the Shares and the Additional Shares as required under Regulation D and to provide a copy thereof promptly upon request of an Investor. The Company shall take such action as the Company shall reasonably determine is necessary in order to obtain an exemption for, or to qualify the Shares and Additional Shares for, sale to the Investor at the Closing and each Additional Closing under applicable securities or "Blue Sky" Laws of the states of the United States, and shall provide evidence of such actions promptly upon request of such Investor.

6.11. **Removal of Legends**. In connection with any sale or disposition of the Shares and the Additional Shares by the Investor pursuant to Rule 144 or pursuant to any other exemption under the Securities Act such that the purchaser thereof acquires freely tradable shares of Common Stock and upon compliance by the Investor with the requirements of this Agreement, if requested by the Investor, the Company shall cause the Transfer Agent to timely remove any restrictive legends related to the book entry account holding such Shares and Additional Shares and make a new, unlegended entry for such book entry Shares and Additional Shares sold or disposed of without restrictive legends. Upon the earlier of such time as the Shares or Additional Shares (i) have been registered under the Securities Act pursuant to an effective registration statement, (ii) have been sold pursuant to Rule 144, or (iii) are eligible for resale under Rule 144(b)(1) or any successor provision, the Company shall (A) deliver to the Transfer Agent irrevocable instructions

that the Transfer Agent shall make a new, unlegended entry for such book entry Shares and Additional Shares, and (B) cause its counsel to deliver to the Transfer Agent one or more opinions to the effect that the removal of such legends in such circumstances may be effected under the Securities Act. The Company shall be responsible for the fees of its Transfer Agent and all Depository Trust Company fees associated with such issuance.

6.12. **Access to Information**.

(a) From the date hereof until the Closing, the Company will make reasonably available to the Investor's representatives, consultants and their respective counsels for inspection, such information and documents as the Investor reasonably requests, and will make available at reasonable times and to a reasonable extent officers and employees of the Company to discuss the business and affairs of the Company.

(b) Following the Closing, if at any time the Investor determines that applicable accounting requirements require consolidation or other integration of the Company's financial information in Investor's financial reports, the Company shall provide the Investor with such information that the Investor may reasonably request to satisfy such obligations within such timeframes as it may reasonably specify to satisfy its financial reporting timelines. Notwithstanding anything to the contrary in this Agreement, the Company consents to the disclosure of such financial information by the Investor as reasonably necessary to comply with Investor's accounting and disclosure requirements. Further, if at any time the Investor or its independent auditor determines that applicable auditing standards require that the Company be included within the scope of such auditor's audit procedures with respect to its audit of the Investor and its Affiliates, the Company shall, at the Investor's sole expense, reasonably cooperate in a timely fashion with reasonable requests to facilitate any such audit procedures.

6.13. **Use of Proceeds**. The Company agrees that the proceeds from the sale and issuance of the Shares and the Additional Shares to the Investor shall be used to fund the costs and expenses of clinical trials and for general working capital and will not be used for purposes of any cash dividend or cash distribution to any stockholder of the Company.

6.14. **Additional Shares**. The Company shall, at all times prior to the Expiration Date, have authorized and reserved for issuance shares of Common Stock sufficient to issue the Additional Shares.

6.15. **Further Assurances**. Each of the parties shall execute such further documents and perform such further acts (including obtaining any consents, exemptions, authorizations or other actions by, or giving notices to, or making any filings with, any Governmental Authority, if necessary) as may be reasonably requested by the other party to fully implement the intent and purpose of this Agreement.

7. **Conditions to Closing**.

7.1. **Investor's Conditions to Closing**. The Investor's obligation to complete the transactions contemplated by this Agreement, including the purchase of the Shares, is subject to

fulfillment or written waiver, at or prior to the Closing (or, with respect to Investor's obligation to complete the purchase of Additional Shares, the applicable Additional Closing), of the following conditions:

(a) **Representations, Warranties and Covenants**. (i) with respect to the Closing, (A) the representations and warranties set forth in Sections 4.1, 4.2, 4.3, 4.4 and 4.5, 4.27 and 4.30 (the "***Company Fundamental Representations***") shall be true and correct in all respects, except for *de minimis* inaccuracies in Section 4.3 which do not result in any increase in the aggregate number of Company Securities outstanding by more than 0.25%, in the aggregate, and (B) the other representations and warranties of the Company contained in this Agreement shall be true and correct (without giving effect to any qualification as to "materiality" or "Material Adverse Effect") in all material respects, in each case of clauses (A) and (B), as of the date hereof and as of the Closing Date (other than such representations and warranties that are expressly made as of another date, in which case as of such other date), and (ii) the covenants and agreements contained in this Agreement to be complied with by the Company on or before the Closing (or the applicable Additional Closing) shall have been complied with in all material respects.

(b) **Company Certificates**. The Investor shall have received from a duly authorized officer of the Company (i) a certificate, dated as of the Closing Date, certifying as to the matters set forth in Section 7.1(a) and (ii) a certificate, dated as of the Closing Date, certifying the resolutions adopted by the Company's board of directors approving the transactions contemplated by this Agreement and certifying the current versions of the Organizational Documents.

(c) **Registration Rights Agreement**. The Investor shall have received an executed counterpart of the Registration Rights Agreement from the Company.

(d) **No Governmental Prohibition**. No Governmental Authority shall have enacted, issued, promulgated, enforced or entered any Law that restrains, enjoins, prohibits or makes illegal the transactions contemplated by this Agreement.

(e) **No Actions**. No Action shall have been commenced or threatened against the Company or the Investor, that challenges, seeks to restrain or seeks to materially and adversely alter the transactions contemplated by this Agreement or that could impose monetary obligations on the Investor.

(f) **Material Adverse Effect**. No Material Adverse Effect shall have occurred since the date of this Agreement and no event shall have occurred that could reasonably be expected to result in a Material Adverse Effect.

(g) **Collaboration Agreement**. The Collaboration Agreement shall be in full force and effect.

(h) **Nasdaq Approval**. The Company shall have filed with Nasdaq a Notification Form: Listing of Additional Shares for the listing of the Shares and, with respect to each

Additional Closing, for the listing of the Additional Shares purchased at such Additional Closing, which shall have been approved by Nasdaq.

(i) **Stop Orders**. No stop order or suspension of trading shall have been imposed by Nasdaq, the Commission or any other Governmental Authority with respect to public trading in the Common Stock.

(j) **Opinion**. The Investor shall have received a customary opinion from Dentons US LLP, counsel for the Company, dated as of the Closing Date, in a form reasonably satisfactory to the Investor.

(k) **Consents**. Any consents, approvals, notices, authorizations, orders, clearances, declarations or filings required for the consummation of the transactions contemplated by this Agreement shall have been made and received (and any waiting periods shall have expired or terminated).

7.2. **Company's Conditions to Closing**. The Company's obligation to complete the transactions contemplated by this Agreement, including the sale of the Shares and Additional Shares, is subject to fulfillment or written waiver, at or prior to the Closing (or, with respect to Company's obligation to effect the sale of Additional Shares, the applicable Additional Closing), of the following conditions:

(a) **Representations, Warranties and Covenants**. (i)(A) The representations and warranties set forth in Sections 5.1, 5.2 and 5.3 (the "***Investor Fundamental Representations***") shall be true and correct in all respects and (B) the other representations and warranties of the Investor contained in this Agreement shall be true and correct (without giving effect to any qualification as to "materiality") in all material respects, in each case of clauses (A) and (B), as of the date hereof and as of the Closing Date and, with respect to each Additional Closing, as of the applicable Additional Closing Date (other than such representations and warranties that are expressly made as of another date, in which case as of such other date) and (ii) the covenants and agreements contained in this Agreement to be complied with by the Investor on or before the Closing (or the applicable Additional Closing) shall have been complied with in all material respects.

(b) **Investor Certificate**. The Company shall have received from a duly authorized officer of the Investor a certificate certifying as to the matters set forth in Section 7.2(a);

(c) **Registration Rights Agreement**. The Investor shall have received an executed counterpart of the Registration Rights Agreement from the Investor.

(d) **No Governmental Prohibition**. No Governmental Authority shall have enacted, issued, promulgated, enforced or entered any Law that restrains, enjoins, prohibits or makes illegal the transactions contemplated by this Agreement.

8. **Termination**.

8.1. **Termination**. This Agreement may only be terminated prior to the Closing:

(a) by the mutual written consent of the Company and the Investor;

(b) by either the Company or the Investor, upon written notice to the other after the three (3) month anniversary of the date of this Agreement (the "***Termination Date***"), if the Transaction shall not have been consummated by the Termination Date pursuant to Section 2; provided, however, that the right to terminate this Agreement under this Section 8.1(b) shall not be available to any party whose failure to fulfill any obligation under this Agreement has been the cause of, or resulted in, the failure to consummate the transactions contemplated hereby prior to the Termination Date;

(c) by either the Company or the Investor in the event that any Law restraining, enjoining, prohibiting or otherwise making illegal the transactions contemplated by this Agreement shall have become final and nonappealable;

(d) by the Company if the Investor shall have breached any of its representations, warranties, covenants or agreements contained in this Agreement which would give rise to the failure of a condition set forth in Section 7, which breach cannot be or has not been cured prior to the Termination Date after the giving of written notice by the Company to the Investor specifying such breach; or

(e) by the Investor if the Company shall have breached any of its representations, warranties, covenants or agreements contained in this Agreement which would give rise to the failure of a condition set forth in Section 7, which breach cannot be or has not been cured prior to the Termination Date after the giving of written notice by the Investor to the Company specifying such breach.

8.2. **Effect of Termination**. In the event of the termination of this Agreement pursuant to Section 8.1 hereof, this Agreement (except for this Section 8.2 and Section 9 (other than Section 9.14) hereof, and any definitions set forth in this Agreement and used in such sections) shall forthwith become void and have no effect, without any liability on the part of any party hereto or its Affiliates; provided, however, that nothing contained in this Section 8.2 shall relieve any party from liability for fraud or any breach of any provision of this Agreement prior to termination.

9. **Miscellaneous**.

9.1. **Equitable Adjustments**. In the event that, prior to the issuance of the Shares or the Additional Shares, there occurs any stock split, stock combination, dividend (whether in securities, cash, or other assets), reorganization, recapitalization, conversion, distribution, exchange, reclassification or other similar event (collectively, a "***Stock Event***"), (i) the amount of Shares or Additional Shares, as applicable, to be issued to the Investor pursuant to this Agreement and the Additional Share Price shall be equitably adjusted to put the Investor in the same position as it would have been had the Shares or Additional Shares, as applicable, been issued to the Investor prior to such event, and (ii) if the Common Stock is converted into or exchanged for securities, cash or other assets, all references herein to the Common Stock shall be deemed to refer to the securities or other assets (including cash) into or for which the Common Stock was converted into or exchanged for. In the event there is any merger or reorganization involving the Company

and the Company is no longer the parent entity of the Company and its Subsidiaries, then all references herein to the Company shall be deemed to refer to the parent entity of the Company and its Subsidiaries.

9.2. **Governing Law; Submission to Jurisdiction**. This Agreement shall be governed by and construed in accordance with the Laws of the State of Delaware, without regard to the conflict of Laws principles thereof that would require the application of the Law of any other jurisdiction. Any Action brought, arising out of, or relating to this Agreement shall be brought in the Court of Chancery of the State of Delaware; provided, however, that if such court does not have jurisdiction over such Action, such Action shall be heard and determined exclusively in any federal court located in the State of Delaware. Each party hereby irrevocably submits to the exclusive jurisdiction of said courts in respect of any claim relating to the validity, interpretation and enforcement of this Agreement, and hereby waives, and agrees not to assert, as a defense in any Action in which any such claim is made that it is not subject thereto or that such Action may not be brought or is not maintainable in such courts, or that the venue thereof may not be appropriate or that this Agreement may not be enforced in or by such courts. The parties hereby consent to and grant the Court of Chancery of the State of Delaware and any federal court sitting in the State of Delaware jurisdiction over such parties and over the subject matter of any such Action and agree that mailing of process or other papers in connection with any such Action in the manner provided in Section 9.5 or in such other manner as may be permitted by Law, shall be valid and sufficient thereof.

9.3. **Waiver of Jury Trial**. EACH OF THE PARTIES HERETO HEREBY IRREVOCABLY AND UNCONDITIONALLY WAIVES TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW ANY RIGHT IT MAY HAVE TO A TRIAL BY JURY WITH RESPECT TO ANY LITIGATION AMONG THE PARTIES DIRECTLY OR INDIRECTLY ARISING OUT OF, UNDER OR IN CONNECTION WITH THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY. EACH OF THE PARTIES HERETO (A) CERTIFIES THAT NO REPRESENTATIVE, AGENT OR ATTORNEY OF ANY OTHER PARTY HAS REPRESENTED, EXPRESSLY OR OTHERWISE, THAT SUCH OTHER PARTY WOULD NOT, IN THE EVENT OF LITIGATION, SEEK TO ENFORCE THAT FOREGOING WAIVER AND (B) ACKNOWLEDGES THAT IT AND THE OTHER PARTY HERETO HAVE BEEN INDUCED TO ENTER INTO THIS AGREEMENT AND THE TRANSACTIONS CONTEMPLATED HEREBY, AS APPLICABLE, BY, AMONG OTHER THINGS, THE MUTUAL WAIVERS AND CERTIFICATIONS IN THIS SECTION.

9.4. **No Waiver, Modifications**. It is agreed that no waiver by a party hereto of any breach or default of any of the covenants or agreements set forth herein shall be deemed a waiver as to any subsequent or similar breach or default. The failure of either party to insist on the performance of any obligation hereunder shall not be deemed a waiver of any such obligation. No amendment, modification, waiver, release or discharge to this Agreement shall be binding upon the parties unless in writing and duly executed by authorized representatives of both parties.

9.5. **Notices**. Any consent, notice, report or other communication required or permitted to be given or made under this Agreement by one of the parties to the other party will be delivered in writing by one of the following means and be effective: (a) upon receipt, if delivered personally; (b) when sent, if sent via e-mail (provided that such sent e-mail is kept on file (whether

electronically or otherwise) by the sending party and the sending party does not immediately receive an automatically generated message from the recipient's e-mail server that such e-mail could not be delivered to such recipient); or (c) when delivered by a reputable, commercial overnight courier; provided in all cases addressed to such other party at its address indicated below, or to such other address as the addressee will have last furnished in writing to the addressor and will be effective upon receipt by the addressee.

If to the Investor:

Ultragenyx Pharmaceutical Inc.
60 Leveroni Court
Novato, CA 94949
Attn: Chief Business Officer
Email: Tkassberg@ultragenyx.com

with a copy (which shall not constitute notice) to:

Shearman & Sterling LLP
599 Lexington Avenue
New York, NY 10022-6069
Attention: Robert Masella
J. Russel Denton
Email: Robert.Masella@Shearman.com
Russ.Denton@Shearman.com

If to the Company:

Arcturus Therapeutics, Inc.
10628 Science Center Drive, Suite 250
San Diego, CA 92121
Attn: Chief Executive Officer
Email: joe@arcturusrx.com

with a copy (which shall not constitute notice) to:

Dentons US LLP
1221 Avenue of the Americas
New York, NY 10020-1089
Attn: Jeffrey Baumel
Email: jeffrey.baumel@dentons.com

Written confirmation of receipt (i) given by the recipient of such notice or (ii) provided by an overnight courier service shall be rebuttable evidence of personal service or receipt from an overnight courier service in accordance with clause (a) or (c) above, respectively. A copy of the e-mail transmission containing the time, date and recipient e-mail address shall be rebuttable evidence of receipt by e-mail in accordance with clause (b) above.

9.6. **Entire Agreement**. This Agreement and the Collaboration Agreement contain the entire agreement among the parties with respect to the subject matter hereof and thereof and supersede all prior and contemporaneous arrangements or understandings, whether written or oral, with respect hereto and thereto.

9.7. **Interpretation and Rules of Construction**. Headings in this Agreement are for convenience of reference only and shall not be considered in construing this Agreement. Whenever the context may require, any pronouns used herein shall include the corresponding masculine, feminine or neuter forms, and the singular form of names and pronouns shall include the plural and vice-versa. References in this Agreement to a section or subsection shall be deemed to refer to a section or subsection of this Agreement unless otherwise expressly stated. Whenever the words "include", "includes" or "including" are used in this Agreement, they are deemed to be followed by the words "without limitation."

9.8. **Severability**. If any provision of this Agreement is held to be illegal, invalid or unenforceable under any present or future Law, and if the rights or obligations of a party under this Agreement will not be materially and adversely affected thereby, (a) such provision shall be fully severable, (b) this Agreement shall be construed and enforced as if such illegal, invalid or unenforceable provision had never comprised a part hereof, (c) the remaining provisions of this Agreement shall remain in full force and effect and shall not be affected by the illegal, invalid or unenforceable provision or by its severance herefrom and (d) in lieu of such illegal, invalid or unenforceable provision, the parties shall negotiate in good faith a substitute legal, valid and enforceable provision as similar in terms to such illegal, invalid or unenforceable provision as possible and as reasonably acceptable to the parties.

9.9. **Assignment**. Except for an assignment by the Investor of this Agreement or any rights hereunder to an Affiliate (which assignment will not relieve the Investor of any obligation hereunder), neither this Agreement nor any of the rights or obligations hereunder may be assigned by either the Investor or the Company without (a) the prior written consent of Company in the case of any assignment by the Investor or (b) the prior written consent of the Investor in the case of an assignment by the Company.

9.10. **Successors and Assigns**. This Agreement shall be binding upon and inure to the benefit of the parties hereto and their respective successors and permitted assigns.

9.11. **Counterparts**. This Agreement may be executed in counterparts, each of which shall be deemed an original but which together shall constitute one and the same instrument. In the event that any signature is delivered by facsimile transmission or by an e-mail which contains a portable document format (.pdf) file of an executed signature page, such executed signature page shall create a valid and binding obligation of the party executing it (or on whose behalf such signature page is executed) with the same force and effect as if such executed signature page were an original thereof.

9.12. **Third Party Beneficiaries**. None of the provisions of this Agreement (other than Section 6.5) shall be for the benefit of or enforceable by any Third Party, including any creditor of any party hereto, except that each Affiliate of the Investor is an express third party beneficiary entitled to enforce this agreement directly against the Company. No Third Party shall obtain any

right under any provision of this Agreement or shall by reason of any such provision make any claim in respect of any debt, liability or obligation (or otherwise) against any party hereto.

9.13. **No Strict Construction**. This Agreement has been prepared jointly and will not be construed against either party. No presumption as to construction of this Agreement shall apply against either party with respect to any ambiguity in the wording of any provision(s) of this Agreement irrespective of which party may be deemed to have authored the ambiguous provision(s).

9.14. **Survival of Warranties**. The representations and warranties of the Company and the Investor contained in this Agreement shall survive the Closing for eighteen (18) months; provided, however, that the Investor Fundamental Representations and the Company Fundamental Representations shall survive indefinitely. It is the intention of the parties to modify the statute of limitations.

9.15. **Specific Performance**. The rights, powers and remedies of the parties under this Agreement are cumulative and not exclusive of any other right, power or remedy which such parties may have under any other agreement or Law. No single or partial assertion or exercise of any right, power or remedy of a party hereunder shall preclude any other or further assertion or exercise thereof. The parties hereby acknowledge and agree that the rights of the parties hereunder are special, unique and of extraordinary character, and that if any party refuses or otherwise fails to act, or to cause its Affiliates to act, in accordance with the provisions of this Agreement, such refusal or failure would result in irreparable injury to the Company or the Investor as the case may be, the exact amount of which would be difficult to ascertain or estimate and the remedies at Law for which would not be reasonable or adequate compensation. Accordingly, if any party refuses or otherwise fails to act, or to cause its Affiliates to act, in accordance with the provisions of this Agreement, then, in addition to any other remedy which may be available to any damaged party at Law or in equity, such damaged party will be entitled to specific performance and injunctive relief, without posting bond or other security, and without the necessity of proving actual or threatened damages, which remedy such damaged party will be entitled to seek in any court of competent jurisdiction.

9.16. **Expenses**. Except as otherwise specified in this Agreement, each party shall pay its own fees and expenses in connection with the preparation, negotiation, execution, delivery and performance of this Agreement.

(*signature page follows*)

IN WITNESS WHEREOF, the parties have executed and delivered this Agreement as of the date first above written.

ARCTURUS THERAPEUTICS HOLDINGS INC.

By: /s/ Joseph E. Payne
Name: Joseph E. Payne
Title: Chief Executive Officer

ARCTURUS THERAPEUTICS LTD.

By: /s/ Joseph E. Payne
Name: Joseph E. Payne
Title: Chief Executive Officer

ULTRAGENYX PHARMACEUTICAL INC.

By: /s/ Emil D. Kakkis
Name: Emil D. Kakkis
Title: President and Chief Executive Officer

THIRD AMENDMENT TO LEASE AGREEMENT

THIS THIRD AMENDMENT TO LEASE AGREEMENT (the "**Third Amendment**") is made as of this 29th day of July, 2019, between **ARE-MA REGION NO. 20, LLC**, a Delaware limited liability company ("**Landlord**"), and **ULTRAGENYX PHARMACEUTICAL INC.**, a Delaware corporation ("**Tenant**").

RECITALS:

A. Tenant and Landlord are parties to that certain Lease Agreement dated as of October 30, 2015, as amended by that certain First Amendment to Lease Agreement dated as of March 20, 2018, and as further amended by that certain Second Amendment to Lease Agreement made as of July 1, 2018 (as amended, the "**Lease**"). Pursuant to the Lease, Tenant leases from Landlord certain premises consisting of approximately 24,038 rentable square feet (the "**Original Premises**") and that certain storage area commonly known as Suite 003 containing approximately 504 rentable square feet ("**Suite 003**") in that certain building located at 19 Presidential Way, Woburn, Massachusetts (the "**Building**"), as more particularly described in the Lease. Capitalized terms used herein without definition shall have the meanings defined for such terms in the Lease.

B. Landlord and Tenant desire, subject to the terms and conditions set forth below, to amend the Lease to, among other things, (i) terminate the lease with respect to Suite 003 and (ii) provide for Tenant to lease those portions of the Building commonly known as Suite 001 containing approximately 504 rentable square feet, Suite 002 containing approximately 567 rentable square feet, Suite 005 containing approximately 544 rentable square feet and Suite 006 containing approximately 821 rentable square feet, as shown on **Exhibit A** attached to this Third Amendment (collectively, the "**Lower Level Premises**").

NOW, THEREFORE, in consideration of the mutual covenants herein expressed and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Tenant and Landlord agree as follows:

1. **Surrender of Suite 003**. Tenant shall voluntarily surrender Suite 003 on or before July 31, 2019 (the "**Termination Date**"). Suite 003 shall be surrendered to Landlord in broom swept clean condition. After the Termination Date, Tenant shall have no further rights of any kind with respect to Suite 003. Nothing herein shall excuse Tenant from its obligations under the Lease with respect to Suite 003 prior to the Termination Date and/or Tenant's other obligations under the Lease, whether before and after the Termination Date, with respect to the Original Premises and the Lower Level Premises.

2. **Lower Level Premises**. Commencing on August 1, 2019 (the "**Lower Level Premises Commencement Date**"), Tenant shall have the right during the Term to use the Lower Level Premises for the storage of Tenant's property and for no other use or purpose. Tenant may not store any Hazardous Materials in the Lower Level Premises. Tenant acknowledges and agrees that, as of the Lower Level Premises Commencement Date, all of Tenant's obligations under the Lease shall apply with respect to the Lower Level Premises as though the Lower Level Premises were part of the Premises, except that Tenant shall not be required to pay Base Rent or Operating Expenses with respect to the Lower Level Premises. Tenant hereby accepts the Lower Level Premises on an "as is" basis and in their condition as of the Lower Level Premises Commencement Date, and Landlord is hereby expressly relieved and released from any duty or obligation to make any improvements or alterations to the Lower Level Premises or to otherwise maintain the Lower Level Premises. The Lower Level Premises shall be surrendered to Landlord at the end of the Term in broom swept clean condition.

3. **Lower Level Premises Fee**. Commencing on the Lower Level Premises Commencement Date, Tenant shall pay to Landlord fees ("**Lower Level Premises Fee**") in the amount of $600 per month for Suite 001, $600 per month for Suite 002, $647.36 per month for Suite 005 and $976.99 per month for Suite 006.

Tenant shall pay to Landlord in advance, without demand, abatement, deduction or set-off, monthly installments of the Lower Level Premises Fee on or before the first day of each calendar month during the Term hereof, in lawful money of the United States of America. Payments of the Lower Level Premises Fee for any fractional calendar month shall be prorated.

4. **OFAC**. Tenant and all beneficial owners of Tenant are currently (a) in compliance with and shall at all times during the Term of the Lease remain in compliance with the regulations of the Office of Foreign Assets Control ("**OFAC**") of the U.S. Department of Treasury and any statute, executive order, or regulation relating thereto (collectively, the "**OFAC Rules**"), (b) not listed on, and shall not during Term of the Lease be listed on, the Specially Designated Nationals and Blocked Persons List, Foreign Sanctions Evaders List, or the Sectoral Sanctions Identification List, which are all maintained by OFAC and/or on any other similar list maintained by OFAC or other governmental authority pursuant to any authorizing statute, executive order, or regulation, and (c) not a person or entity with whom a U.S. person is prohibited from conducting business under the OFAC Rules.

5. **Brokers**. Landlord and Tenant each represents and warrants that it has not dealt with any broker, agent or other person (collectively, "**Broker**") in connection with the transaction reflected in this Third Amendment and that no Broker brought about this transaction. Landlord and Tenant each hereby agree to indemnify and hold the other harmless from and against any claims by any Broker, other than the brokers, if any, named in this Third Amendment, claiming a commission or other form of compensation by virtue of having dealt with Landlord or Tenant, as applicable, with regard to this Third Amendment.

6. **Miscellaneous**.

a. This Third Amendment is the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior and contemporaneous oral and written agreements and discussions. This Third Amendment may be amended only by an agreement in writing, signed by the parties hereto.

b. This Third Amendment is binding upon and shall inure to the benefit of the parties hereto, and their respective successors and assigns.

c. This Third Amendment may be executed in 2 or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Counterparts may be delivered via facsimile, electronic mail (including pdf or any electronic signature process complying with the U.S. federal ESIGN Act of 2000) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes. Electronic signatures shall be deemed original signatures for purposes of this Third Amendment and all matters related thereto, with such electronic signatures having the same legal effect as original signatures.

d. Except as amended and/or modified by this Third Amendment, the Lease is hereby ratified and confirmed and all other terms of the Lease shall remain in full force and effect, unaltered and unchanged by this Third Amendment. In the event of any conflict between the provisions of this Third Amendment and the provisions of the Lease, the provisions of this Third Amendment shall prevail. Whether or not specifically amended by this Third Amendment, all of the terms and provisions of the Lease are hereby amended to the extent necessary to give effect to the purpose and intent of this Third Amendment.

[Signatures are on the next page]

IN WITNESS WHEREOF, the parties have caused their duly authorized representatives to execute this Third Amendment as of the date first written above.

TENANT:

ULTRAGENYX PHARMACEUTICAL INC.,
a Delaware corporation

By: /s/ P.K. Tandon
Print Name: P.K. Tandon
Its:

LANDLORD:

ARE-MA REGION NO. 20, LLC,
a Delaware limited liability company

By: ALEXANDRIA REAL ESTATE EQUITIES, L.P.,
a Delaware limited partnership,
managing member

By:
QRS CORP.,
a Maryland
corporation,
general
partner

/s/ Jackie Clem

Print Name: Jackie Clem

Its: RE Legal Affairs

FOURTH AMENDMENT TO LEASE AGREEMENT

THIS FOURTH AMENDMENT TO LEASE AGREEMENT (this "**Fourth Amendment**") is made as of this 31st day of March, 2020, between **ARE-MA REGION NO. 20, LLC**, a Delaware limited liability company ("**Landlord**"), and **ULTRAGENYX PHARMACEUTICAL INC.**, a Delaware corporation ("**Tenant**").

RECITALS:

A. Tenant and Landlord are parties to that certain Lease Agreement dated as of October 30, 2015, as amended by that certain First Amendment to Lease Agreement dated as of March 20, 2018, as further amended by that certain Second Amendment to Lease Agreement dated as of July 1, 2018 (the "**Second Amendment**"), and as further amended by that certain Third Amendment to Lease Agreement dated as of July 29, 2019 (the "**Third Amendment**") (as amended, the "**Lease**"). Pursuant to the Lease, Tenant leases from Landlord certain premises consisting of approximately 24,038 rentable square feet (the "**Existing Premises**") in that certain building located at 19 Presidential Way, Woburn, Massachusetts (the "**Building**"), as more particularly described in the Lease. Capitalized terms used herein without definition shall have the meanings defined for such terms in the Lease.

B. Landlord and Tenant acknowledge and agree that, concurrently with the mutual execution and delivery of this Fourth Amendment by Landlord and Tenant, Landlord is entering into a termination agreement with Enko Chem, Inc. ("**Existing Tenant**"), the existing tenant of the Second Expansion Premises (as defined below), pursuant to which Landlord and Existing Tenant have agreed to accelerate the expiration date of Existing Tenant's lease with respect to the Second Expansion Premises.

C. Landlord and Tenant desire, subject to the terms and conditions set forth below, to amend the Lease to, among other things, expand the size of the Existing Premises by adding that portion of the third floor of the Building containing approximately 7,805 rentable square feet, as shown on **Exhibit A** attached to this Fourth Amendment (the "**Second Expansion Premises**")

NOW, THEREFORE, in consideration of the mutual covenants herein expressed and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Tenant and Landlord agree as follows:

1. **Second Expansion Premises**. In addition to the Existing Premises, commencing on the Second Expansion Premises Commencement Date (as defined below), Landlord leases to Tenant, and Tenant leases from Landlord, the Second Expansion Premises.

2. **Delivery**. Landlord shall use reasonable efforts to deliver the Second Expansion Premises to Tenant on or before July 1, 2020. If Landlord fails to deliver the Second Expansion Premises to Tenant on or before July 1, 2020, Landlord shall not be liable to Tenant for any loss or damage resulting therefrom, and the Lease with respect to the Second Expansion Premises shall not be void or voidable except as provided herein. If Landlord does not deliver the Second Expansion Premises to Tenant by September 1, 2020, for any reason other than Force Majeure delays, this Fourth Amendment may be terminated by Tenant by written notice to Landlord, and if so terminated by Tenant, this Fourth Amendment shall be null and void and neither Landlord nor Tenant shall have any further rights, duties or obligations under this Fourth Amendment, except with respect to provisions which expressly survive termination of this Fourth Amendment. If Tenant does not elect to void this Fourth Amendment on or before September 10, 2020, such right to void this Fourth Amendment shall be waived and this Fourth Amendment shall remain in full force and effect. Landlord and Tenant acknowledge and agree that, notwithstanding anything to the contrary contained in this Fourth Amendment or in the Lease, the failure of Existing Tenant to surrender the Second Expansion Premises shall in no event constitute a Force Majeure delay.

The "**Second Expansion Premises Commencement Date**" shall be the date that Landlord delivers the Second Expansion Premises to Tenant.

Upon the request of Landlord, Tenant shall execute and deliver a written acknowledgment of the Second Expansion Premises Commencement Date in substantially the form of the "Acknowledgement of Second Expansion Premises Commencement Date" attached hereto as **Exhibit B**; provided, however, Tenant's failure to execute and deliver such acknowledgment shall not affect Landlord's or Tenant's rights hereunder.

Except as otherwise expressly set forth in the Lease or this Fourth Amendment: (i) Tenant shall accept the Second Expansion Premises in their condition as of the Second Expansion Premises Commencement Date; (ii) Landlord shall have no obligation for any defects in the Second Expansion Premises; and (iii) Tenant's taking possession of the Second Expansion Premises shall be conclusive evidence that Tenant accepts the Second Expansion Premises and that the Second Expansion Premises were in good condition at the time possession was taken.

For the period of 60 consecutive days after the Second Expansion Premises Commencement Date, Landlord shall, at its sole cost and expense (which shall not constitute an Operating Expense), be responsible for any repairs that are required to be made to the Building Systems serving only the Second Expansion Premises, unless Tenant or any Tenant Party was responsible for the cause of such repair, in which case Tenant shall pay the cost.

Tenant agrees and acknowledges that neither Landlord nor any agent of Landlord has made any representation or warranty with respect to the condition of all or any portion of the Second Expansion Premises, and/or the suitability of the Second Expansion Premises for the conduct of Tenant's business, and Tenant waives any implied warranty that the Second Expansion Premises are suitable for the Permitted Use.

3. **Premises and Rentable Area of Premises**. Commencing on the Second Expansion Premises Commencement Date, the defined terms "**Premises**" and "**Rentable Area of Premises**" on page 1 of the Lease shall be deleted in their entirety and replaced with the following:

> "**Premises:** That portion of the Building, consisting of (i) approximately 17,475 rentable square feet of laboratory/office space on the second floor of the Building (the "**Original Premises**"), (ii) approximately 108 rentable square feet of storage space on the first floor of the Building (the "**Storage Premises**"), (iii) approximately 6,455 rentable square feet of laboratory/office space on the third floor of the Building (the "**Expansion Premises**"), and (iv) approximately 7,805 rentable square feet of laboratory/office space on the third floor of the Building (the "**Second Expansion Premises**"), all as determined by Landlord, as shown on **Exhibit A**."
>
> "**Rentable Area of Premises:** 31,843 sq. ft."

As of the Second Expansion Premises Commencement Date, **Exhibit A** to the Lease shall be amended to include the Second Expansion Premises as shown on **Exhibit A** attached to this Fourth Amendment.

4. **Base Rent**.

a. **Existing Premises**. Tenant shall continue to pay Base Rent with respect to the Existing Premises as provided for under the Lease through March 31, 2021. Commencing on April 1, 2021, Tenant shall pay Base Rent for the Existing Premises in the amount of $34.00 per rentable square foot of the Existing Premises per year. Base Rent payable with respect to the Existing Premises shall increase on April 1, 2022, and on each April 1st thereafter through the Extended Expiration

Date (as defined below in Section 5)(each, an "**Existing Premises Adjustment Date**") by multiplying the Base Rent payable with respect to the Existing Premises immediately before such Existing Premises Adjustment Date by 3% and adding the resulting amount to the Base Rent payable with respect to the Existing Premises immediately before such Existing Premises Commencement Date.

b. **Second Expansion Premises**. Commencing on the Second Expansion Premises Commencement Date, Tenant shall pay Base Rent with respect to the Second Expansion Premises in the amount of $41.00 per rentable square foot of the Second Expansion Premises per year. Base Rent payable with respect to the Second Expansion Premises shall be increased on each annual anniversary of the Second Expansion Premises Commencement Date (each, a "**Second Expansion Premises Adjustment Date**") by multiplying the Base Rent payable with respect to the Second Expansion Premises immediately before such Second Expansion Premises Adjustment Date by 3% and adding the resulting amount to the Base Rent payable with respect to the Second Expansion Premises immediately before such Second Expansion Premises Adjustment Date.

5. **Base Term**. Commencing on the Second Expansion Premises Commencement Date, the defined term "**Base Term**" on page 1 of the Lease shall be deleted in its entirety and replaced with the following"

"**Base Term:** Commencing (i) with respect to Original Premises on the Commencement Date, (ii) with respect to the Expansion Premises on the Expansion Premises Commencement Date, and (iii) with respect to the Second Expansion Premises on the Second Expansion Premises Commencement Date, and ending with respect to the entire Premises on April 30, 2025 (the "**Extended Expiration Date**")."

6. **Tenant's Share**. Commencing on the Second Expansion Premises Commencement Date, the defined term "**Tenant's Share of Operating Expenses**" on page 1 of the Lease shall be deleted in its entirety and replaced with the following:

"**Tenant's Share of Operating Expenses:** 21.98%"

7. **Premises Improvements**. Commencing on the Second Expansion Premises Commencement Date, Landlord shall make available to Tenant a tenant improvement allowance in the amount of $15.00 per rentable square foot of the Premises, or $477,645.00 in the aggregate (the "**Fourth Amendment Improvement Allowance**") for the design and construction of fixed and permanent improvements desired by and performed by Tenant and reasonably acceptable to Landlord in the Premises (the "**Premises Improvements**"), which Premises Improvements shall be constructed pursuant to a scope of work reasonably acceptable to Landlord and Tenant. The Fourth Amendment Improvement Allowance shall be available only for the design and construction of the Premises Improvements. The Fourth Amendment Improvement Allowance may not be used to purchase any furniture, personal property or other non-Building System materials or equipment, except that Tenant may use a portion of the Fourth Amendment Improvement Allowance for Tenant's tele/data cabling. Tenant acknowledges that upon the expiration or earlier termination of the Term of the Lease, the Premises Improvements shall become the property of Landlord and may not be removed by Tenant. Except for the Fourth Amendment Improvement Allowance, Tenant shall be solely responsible for all of the costs of the Premises Improvements. The Premises Improvements shall be treated as Alterations and shall be undertaken pursuant to Section 12 of the Lease. The contractor for the Second Amendment Improvements shall be selected and engaged by Tenant, subject to Landlord's approval, which approval shall not be unreasonably withheld, conditioned or delayed. Prior to the commencement of the Premises Improvements, Tenant shall deliver to Landlord a copy of any contract with Tenant's contractors, and certificates of insurance from any contractor performing any part of the Premises Improvements evidencing industry standard commercial general liability, automotive liability, "builder's risk", and workers' compensation insurance. Tenant shall cause the general contractor to provide a certificate of insurance naming Landlord, Alexandria Real Estate Equities, Inc., and Landlord's lender (if any) as additional insureds for the general contractor's liability coverages required above.

During the course of design and construction of the Premises Improvements, Landlord shall reimburse Tenant for the cost of the Premises Improvements once a month against a draw request in Landlord's standard form, containing evidence of payment of the applicable costs and such certifications, lien waivers (including a conditional lien release for each progress payment and unconditional lien releases for the prior month's progress payments), inspection reports and other matters as Landlord customarily and reasonably obtains, to the extent of Landlord's approval thereof for payment, no later than 30 days following receipt of such draw request. Upon completion of the Premises Improvements (and prior to any final disbursement of the Fourth Amendment Improvement Allowance) Tenant shall deliver to Landlord the following items: (i) sworn statements setting forth the names of all contractors and subcontractors who did work on the Premises Improvements and final lien waivers from all such contractors and subcontractors; and (ii) "as built" plans, if available, for Premises Improvements. Notwithstanding the foregoing, if the cost of the Premises Improvements exceeds the Fourth Amendment Improvement Allowance, Tenant shall be required to pay such excess in full prior to Landlord having any obligation to fund any remaining portion of the Fourth Amendment Improvement Allowance. The Fourth Amendment Improvement Allowance shall only be available for use by Tenant for the construction of the Premises Improvements from the date of this Fourth Amendment through the date that is 36 months after the date of this Fourth Amendment (the "**Outside Fourth Amendment Improvement Allowance Date**"). Any portion of the Fourth Amendment Improvement Allowance which has not been properly requested by Tenant from Landlord on or before the Outside Fourth Amendment Improvement Allowance Date shall be forfeited and shall not be available for use by Tenant.

Landlord and Tenant acknowledge that Tenant did not use any of the Improvement Allowance made available to Tenant pursuant to the Second Amendment. Notwithstanding anything to the contrary contained in the Second Amendment or in this Fourth Amendment, in addition to the Fourth Amendment Improvement Allowance, Tenant shall have the right to use the Improvement Allowance in the amount of $64,550.00 toward the cost of the Premises Improvements prior to the Outside Fourth Amendment Improvement Allowance Date.

8. **Right to Expand**.

(a) **Expansion in the Building**. Following the Second Expansion Premises Commencement Date, Tenant shall have the one-time right, but not the obligation, to expand the Premises (the "**Expansion Right**") to include the Expansion Space upon the terms and conditions set forth in this Section. For purposes of this Section 8(a), "**Expansion Space**" shall mean that certain space on the second floor of the Building consisting of approximately 9,521 rentable square feet commonly known as Suite 201, which is not occupied by a tenant or which is occupied by a then-existing tenant whose lease is being terminated or whose lease is expiring within 9 months or less and such tenant does not wish to renew (whether or not such tenant has a right to renew) its occupancy of such space. If all or a portion of the Expansion Space become available Landlord shall, at such time as Landlord shall elect so long as Tenant's rights hereunder are preserved, deliver to Tenant written notice (the "**Expansion Notice**") of such Expansion Space, together with the terms and conditions on which Landlord is prepared to lease Tenant the Expansion Space. Tenant shall be entitled to exercise its right under this Section 8(a) only with respect to the entire Expansion Space identified in the Expansion Notice ("**Identified Expansion Space**"). Tenant shall have 10 business days following delivery of the Expansion Notice to deliver to Landlord written notification of Tenant's exercise of the Expansion Right ("**Exercise Notice**") with respect to the Identified Expansion Space. Tenant shall be entitled to lease the Identified Expansion Space upon the terms and conditions set forth in the Expansion Notice and otherwise consistent with the terms of the Lease. The Term of the Lease with respect to the Identified Expansion Space may not be co-terminous with the Term of the Lease with respect to the then-existing Premises, but in no event shall the Term of the lease with respect to the Identified Expansion Space be longer than 7 years from the date on which the Lease commences with respect to the Identified Expansion Space. Notwithstanding anything to the contrary contain herein, in no event shall the Fourth Amendment Improvement Allowance apply with respect to the Identified Expansion Space. If Tenant fails to deliver an Exercise Notice to Landlord for the Identified Expansion Space within the required 10

business day period, Tenant shall be deemed to have waived its rights under this Section 8(a) to lease the Expansion Space, and Landlord shall have the right to lease the Expansion Space to any third party on any terms and conditions acceptable to Landlord. Notwithstanding anything to the contrary contained herein, Tenant shall have no right to exercise the Expansion Right and the provisions of this Section 8(a) shall no longer apply after the date that is 9 months prior to the Extended Expiration Date if Tenant has not exercised its Extension Right pursuant to Section 39 of the original Lease.

(b) **Amended Lease**. If: (i) Tenant fails to timely deliver an Exercise Notice, or (ii) following Tenant's delivery of an exercise notice to Landlord, Landlord tenders to Tenant an amendment to the Lease for the rental of the Identified Expansion Space reasonably acceptable to Landlord and Tenant, each in their reasonable discretion, and Tenant fails to execute such Lease amendment within 10 days following such tender, Tenant shall be deemed to have waived its right to lease the Identified Expansion Space.

(c) **Exceptions**. Notwithstanding the above, the Expansion Right shall, at Landlord's option, not be in effect and may not be exercised by Tenant:

(ii) during any period of time that Tenant is in default (following any applicable notice and cure periods) under any provision of the Lease; or

(ii) if Tenant has been in default (following any applicable notice and cure periods) under any provision of the Lease 3 or more times, whether or not the defaults (following any applicable notice and cure periods) are cured, during the 12 month period prior to the date on which Tenant seeks to exercise the Expansion Right.

(d) **Termination**. The Expansion Right shall, at Landlord's option, terminate and be of no further force or effect even after Tenant's due and timely exercise of the Expansion Right, if, after such exercise, but prior to the commencement date of the lease of the Identified Expansion Space, (i) Tenant fails to timely cure any default by Tenant (following any applicable notice and cure periods) under the Lease; or (ii) Tenant has defaulted (following any applicable notice and cure periods) 3 or more times during the period from the date of the exercise of the Expansion Right to the date of the commencement of the lease of the Identified Expansion Space, whether or not such defaults (following any applicable notice and cure periods) are cured.

(e) **Rights Personal**. The Expansion Right is personal to Tenant and is not assignable without Landlord's consent, which may be granted or withheld in Landlord's sole discretion separate and apart from any consent by Landlord to an assignment of Tenant's interest in the Lease, except that they may be assigned in connection with any Permitted Assignment of the Lease.

(f) **No Extensions**. The period of time within which the Expansion Right may be exercised shall not be extended or enlarged by reason of Tenant's inability to exercise the Expansion Right.

9. **Lower Level Premises**. For the avoidance of doubt, the terms of the Third Amendment shall continue to apply with respect to the Lower Level Premises.

10. **Parking**. Subject to the terms and conditions of Section 10 of the Lease, Tenant shall have the right, at no additional cost, to use its pro rata share of parking spaces with respect to the Second Expansion Premises, which parking spaces shall be in those areas of the Project designated for non-reserved parking.

11. **Signage**. Suite entry signage with respect to the Second Expansion Premises and signage on the directory tablet serving the Building shall be inscribed, painted or affixed for Tenant by Landlord, at Landlord's cost.

12. **OFAC**. Tenant and Landlord are currently (a) in compliance with and shall at all times during the Term of the Lease remain in compliance with the regulations of the Office of Foreign Assets Control ("**OFAC**") of the U.S. Department of Treasury and any statute, executive order, or regulation relating thereto (collectively, the "**OFAC Rules**"), (b) not listed on, and shall not during Term of the Lease be listed on, the Specially Designated Nationals and Blocked Persons List, Foreign Sanctions Evaders List, or the Sectoral Sanctions Identification List, which are all maintained by OFAC and/or on any other similar list maintained by OFAC or other governmental authority pursuant to any authorizing statute, executive order, or regulation, and (c) not a person or entity with whom a U.S. person is prohibited from conducting business under the OFAC Rules.

13. **Brokers**. Landlord and Tenant each represents and warrants that it has not dealt with any broker, agent or other person (collectively, "**Broker**") in connection with the transaction reflected in this Fourth Amendment and that no Broker brought about this transaction, other than Colliers International and CBRE. Landlord and Tenant each hereby agree to indemnify and hold the other harmless from and against any claims by any Broker, other than Colliers International and CBRE, claiming a commission or other form of compensation by virtue of having dealt with Landlord or Tenant, as applicable, with regard to this Fourth Amendment.

14. **Miscellaneous**.

(a) This Fourth Amendment is the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior and contemporaneous oral and written agreements and discussions. This Fourth Amendment may be amended only by an agreement in writing, signed by the parties hereto.

(b) This Fourth Amendment is binding upon and shall inure to the benefit of the parties hereto, and their respective successors and assigns.

(c) This Fourth Amendment may be executed in 2 or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Counterparts may be delivered via facsimile, electronic mail (including pdf or any electronic signature process complying with the U.S. federal ESIGN Act of 2000) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes. Electronic signatures shall be deemed original signatures for purposes of this Fourth Amendment and all matters related thereto, with such electronic signatures having the same legal effect as original signatures.

(d) Except as amended and/or modified by this Fourth Amendment, the Lease is hereby ratified and confirmed and all other terms of the Lease shall remain in full force and effect, unaltered and unchanged by this Fourth Amendment. In the event of any conflict between the provisions of this Fourth Amendment and the provisions of the Lease, the provisions of this Fourth Amendment shall prevail. Whether or not specifically amended by this Fourth Amendment, all of the terms and provisions of the Lease are hereby amended to the extent necessary to give effect to the purpose and intent of this Fourth Amendment.

[Signatures are on the next page]

IN WITNESS WHEREOF, the parties have caused their duly authorized representatives to execute this Fourth Amendment as of the date first written above.

TENANT:

ULTRAGENYX PHARMACEUTICAL INC.,
a Delaware corporation

By: /s/ Thomas Kassberg
Print Name: Thomas Kassberg
Its: Chief Business Officer

LANDLORD:

ARE-MA REGION NO. 20, LLC,
a Delaware limited liability company

By: ALEXANDRIA REAL ESTATE EQUITIES, L.P.,
a Delaware limited partnership,
managing member

By: QRS CORP.,
a Maryland corporation,
general partner

/s/ Kristin Childs
Print Name: Kristin Childs
Vice President, RE Legal Affairs

EXHIBIT A

SECOND EXPANSION PREMISES

EXHIBIT B

ACKNOWLEDGMENT OF SECOND EXPANSION PREMISES COMMENCEMENT DATE

This **ACKNOWLEDGMENT OF SECOND EXPANSION PREMISES COMMENCEMENT DATE** is made this _____ day of _____, ____, between **ARE-MA REGION NO. 20, LLC**, a Delaware limited liability company ("**Landlord**"), and **ULTRAGENYX PHARMACEUTICAL INC.**, a Delaware corporation ("**Tenant**"), and is attached to and made a part of that certain Lease Agreement dated as of October 30, 2015, as amended by that certain First Amendment to Lease Agreement dated as of March 20, 2018, as further amended by that certain Second Amendment to Lease Agreement dated as of July 1, 2018, as further amended by that certain Third Amendment to Lease Agreement dated as of July 29, 2019, and as further amended by that certain Fourth Amendment to Lease Agreement dated as of March ___, 2020 (as amended, the "**Lease**"), by and between Landlord and Tenant. Any initially capitalized terms used but not defined herein shall have the meanings given them in the Lease.

Landlord and Tenant hereby acknowledge and agree, for all purposes of the Lease, that the Second Expansion Premises Commencement Date is _____, _____, and the termination date of the Base Term of the Lease shall be midnight on April 30, 2025. In case of a conflict between the terms of the Lease and the terms of this Acknowledgment of Second Expansion Premises Commencement Date, this Acknowledgment of Second Expansion Premises Commencement Date shall control for all purposes.

IN WITNESS WHEREOF, Landlord and Tenant have executed this ACKNOWLEDGMENT OF SECOND EXPANSION PREMISES COMMENCEMENT DATE to be effective on the date first above written.

LANDLORD: **ARE-MA REGION NO. 20, LLC**,
a Delaware limited liability company

By: ALEXANDRIA REAL ESTATE EQUITIES, L.P.,
a Delaware limited partnership,
its managing member

By: ARE-QRS CORP.,
a Maryland corporation,
its general partner

By:
Its:

TENANT: **ULTRAGENYX PHARMACEUTICAL INC.**,

a Delaware corporation

By:
Name:
Title:

Exhibit 31.1

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Emil D. Kakkis, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Ultragenyx Pharmaceutical Inc.;

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

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

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

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

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

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

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

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

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

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

Dated: July 30, 2020

/s/ Emil D Kakkis
Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Shalini Sharp, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Ultragenyx Pharmaceutical Inc.;

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

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

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

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

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

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

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

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

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

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

Dated: July 30, 2020

/s/ Shalini Sharp
Shalini Sharp
Chief Financial Officer and Executive Vice President
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002 (18 U.S.C. SECTION 1350)

In connection with the accompanying Quarterly Report of Ultragenyx Pharmaceutical Inc. (the "Company") on Form 10-Q for the quarter ended June 30, 2020 (the "Report"), I, Emil D. Kakkis, M.D., Ph.D., as President and Chief Executive Officer of the Company, and Shalini Sharp, as Chief Financial Officer and Executive Vice President of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

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

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

Dated: July 30, 2020

/s/ Emil D. Kakkis
Emil D. Kakkis, M.D., Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Dated: July 30, 2020

/s/ Shalini Sharp
Shalini Sharp
Chief Financial Officer and Executive Vice President
(Principal Financial Officer)