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, 2017

OR

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

For the transition period from_____to_____

Commission File Number: 001-37601

DIMENSION THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**46-3942159**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
840 Memorial Drive Cambridge, MA	**02139**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 401-0011

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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or 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	☐ (Do not check if a small reporting company)	Small 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 ☒

The number of shares of Registrant's Common Stock outstanding as of August 1, 2017 was 25,052,628.

INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains "forward-looking statements" that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Quarterly Report on Form 10-Q, including statements regarding our future results of operations and financial position, strategy and plans and our expectations for future operations, are forward- looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. The words "anticipate," "believe," "contemplates," "continue," "could," "design," "estimate," "expect," "intend," "likely," "may," "ongoing," "plan," "potential," "predict," "project," "will," "would," "seek," "should," "target," or the negative version of these words and similar expressions are intended to identify forward-looking statements. We have based these forward-looking statements on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, strategy, short- and long-term business operations and objectives and financial needs. These forward-looking statements are subject to a number of risks, uncertainties, assumptions and other important factors, including those described in the section titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in this Quarterly Report on Form 10-Q and Annual Report on Form 10-K for the fiscal year ended on December 31, 2016. In light of these risks, uncertainties, assumptions and other factors, the forward-looking events and circumstances discussed in this Quarterly Report on Form 10-Q or our Annual Report on Form 10-K for the fiscal year ended on December 31, 2016 may not occur, and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

Given these uncertainties, you should not place undue reliance on these forward-looking statements.

Forward-looking statements include, but are not limited to, statements about:

- the timing, progress and results of preclinical studies and clinical trials for our DTX301, DTX401, DTX201, and DTX701 programs and product candidates and our other product candidates, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the initial or final results of the trials will become available, and the status of our research and development programs;
- the timing, scope or likelihood of regulatory filings and approvals, including timing of our biologics license application (BLA) filing for, and final FDA approval of, our programs and product candidates;
- our ability to develop and advance product candidates into, and successfully complete, clinical studies;
- our expectations regarding the size of the patient populations for our product candidates, if approved for commercial use;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model and our strategic plans for our business, product candidates and technology;
- the scalability and commercial viability of our manufacturing methods and processes;
- the rate and degree of market acceptance and clinical utility of our product candidates, in particular, and gene therapy, in general;
- the potential benefits of our existing collaboration with Bayer and our ability to establish or maintain other collaborations or strategic relationships or obtain additional funding;
- our competitive position;
- the scope of protection we and/or our licensors are able to establish and maintain for intellectual property rights covering our product candidates;
- developments and projections relating to our competitors and our industry;
- our estimates regarding expenses, future revenue, capital requirements and needs for financing;
- the impact of laws and regulations; and
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, level of activity, performance or achievements. Any forward-looking statement made by us in this Quarterly Report on Form 10-Q speaks only as of the date of this report. Except as required by law, we disclaim any duty to update any of these forward-looking statements after the date such statements are made, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

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PART I—FINANCIAL INFORMATION

Item 1. Condensed Consolidated Unaudited Financial Statements.

DIMENSION THERAPEUTICS, INC.

CONDENSED CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share amounts)
(Unaudited)

	June 30, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 25,062	$ 30,234
Marketable securities	22,428	47,715
Accounts receivable	3,097	1,885
Prepaid expenses and other current assets	6,075	5,484
Total current assets	56,662	85,318
Property and equipment, net	7,344	8,402
Deferred offering costs	205	145
Total assets	$ 64,211	$ 93,865
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,335	$ 2,368
Accrued expenses and other current liabilities	3,339	7,247
Deferred revenue	9,867	8,663
Notes payable	2,455	2,361
Total current liabilities	16,996	20,639
Deferred revenue, net of current portion	7,385	8,663
Notes payable, net of discount and current portion	3,321	4,169
Other liabilities	436	453
Total liabilities	28,138	33,924
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized at June 30, 2017 and December 31, 2016; zero shares issued or outstanding at June 30, 2017 and December 31, 2016.	—	—
Common stock, $0.0001 par value; 150,000,000 shares authorized as of June 30, 2017 and December 31, 2016; 25,043,506 shares issued and outstanding as of June 30, 2017 and December 31, 2016.	2	2
Additional paid-in capital	162,117	160,185
Accumulated deficit	(125,996)	(100,195)
Accumulated other comprehensive loss	(50)	(51)
Total stockholders' equity	36,073	59,941
Total liabilities and stockholders' equity	$ 64,211	$ 93,865

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

DIMENSION THERAPEUTICS, INC.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share amounts)

(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
Revenue	$ 4,369	$ 2,371	$ 7,987	$ 4,577
Operating expenses:				
Research and development	14,089	11,240	27,803	20,045
General and administrative	2,610	3,236	6,042	6,177
Total operating expenses	16,699	14,476	33,845	26,222
Loss from operations	(12,330)	(12,105)	(25,858)	(21,645)
Interest income, net	21	6	57	35
Net loss	$ (12,309)	$ (12,099)	$ (25,801)	$ (21,610)
Net loss per share — basic and diluted	$ (0.49)	$ (0.49)	$ (1.03)	$ (0.87)
Weighted average common shares outstanding — basic and diluted	25,002,532	24,899,479	24,992,162	24,885,823
Comprehensive loss:				
Net loss	$ (12,309)	$ (12,099)	$ (25,801)	$ (21,610)
Other comprehensive loss:				
Unrealized gain (loss) on marketable securities	1	—	(50)	—
Total other comprehensive loss	1	—	(50)	—
Total comprehensive loss	$ (12,308)	$ (12,099)	$ (25,851)	$ (21,610)

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

DIMENSION THERAPEUTICS, INC.

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)
(Unaudited)

	Six Months Ended June 30,	
	2017	**2016**
Cash flows from operating activities:		
Net loss	$ (25,801)	$ (21,610)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	1,082	638
Stock-based compensation expense	1,932	1,330
Non-cash interest expense	90	29
Amortization of premium on marketable securities	37	—
Changes in operating assets and liabilities:		
Accounts receivable	(1,212)	(1,176)
Prepaid expenses and other current assets	(591)	(967)
Accounts payable	(1,033)	(1,186)
Accrued expenses and other current liabilities	(3,908)	1,116
Deferred revenue	(74)	23
Other liabilities	(17)	477
Net cash used in operating activities	(29,495)	(21,326)
Cash flows from investing activities:		
Maturities of marketable securities	25,251	—
Purchases of property and equipment	(24)	(4,906)
Net cash provided (used) in investing activities	25,227	(4,906)
Cash flows from financing activities:		
Proceeds from exercise of common stock options	—	10
Proceeds from issuance of notes payable	276	4,117
Repayment of notes payable	(1,120)	(291)
Payments of offering costs	(60)	—
Net cash provided (used) by financing activities	(904)	3,836
Net decrease in cash and cash equivalents	(5,172)	(22,396)
Cash and cash equivalents at beginning of period	30,234	127,047
Cash and cash equivalents at end of period	$ 25,062	$ 104,651
Supplemental disclosure of cash flow information:		
Interest paid	$ 101	$ 37
Supplemental disclosure of non-cash investing and financing activities:		
Purchases of property and equipment included in accounts payable, accrued expenses and other liabilities	$ —	$ 326

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

DIMENSION THERAPEUTICS, INC.

NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

(Amounts in thousands, except share and per share amounts) (Unaudited)

1. Nature of the Business and Basis of Presentation

Dimension Therapeutics, Inc. ("we" or the "Company") was incorporated in Delaware on June 20, 2013. The Company is a leader in discovering and developing new therapeutic products for people living with devastating rare and metabolic diseases associated with the liver, based on the most advanced, mammalian adeno-associated virus (AAV) gene delivery technology. The liver is a vital organ that plays an important role in human metabolism and key physiologic functions, and is the target organ for our initial programs: OTC deficiency, GSDIa, Wilson disease, and hemophilia A.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and ability to secure additional capital to fund operations. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

In accordance with ASC 205-40, Going Concern, the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the condensed consolidated financial statements are issued. As of June 30, 2017, the Company had an accumulated deficit of $125,996. During the three and six months ended June 30, 2017, the Company incurred a loss of $12,309 and $25,801, respectively, and during the six months ended June 30, 2017, the Company used $29,495 of cash in operations. The Company expects to continue to generate operating losses in the foreseeable future. The Company expects that its cash, cash equivalents and marketable securities of $47,490 as of June 30, 2017, together with the receipt of contingent payments expected to be received in connection with our collaboration with Bayer, including reimbursements and $15,000 in milestones, and cost management initiatives, will be sufficient to fund its operating expenses and capital expenditure requirements for at least the next 12 months from issuance of the financial statements. Without the Bayer milestone payments, the Company's existing capital resources, as of June 30, 2017 would not be sufficient to fund its operating expenses and capital expenditure requirements through August 8, 2018, or 12 months from issuance of the condensed consolidated financial statements. If the Company does not obtain the Bayer milestone payments, the Company would be forced to delay, reduce or eliminate certain research and development programs, reduce or eliminate discretionary operating expenses, delay product portfolio expansion, which could adversely affect its business prospects. In addition, the Company will seek additional funding through public or private financings, debt financing, collaboration agreements or government grants. The inability to obtain funding, as and when needed, would have a negative impact on the Company's financial condition and ability to pursue its business strategies. Such contingency plans have not been finalized and are not considered probable for purposes of ASC 205-40. As neither the receipt of the Bayer milestone payments nor management's contingency plans to mitigate the risk and extend cash resources through August 8, 2018, are considered probable under ASC 205-40, substantial doubt is deemed to exist about the Company's ability to continue as a going concern.

The condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP").

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The accompanying condensed consolidated financial statements reflect the operations of Dimension Therapeutics, Inc. and Dimension Securities Corporation, our wholly-owned subsidiary. All intercompany accounts and transactions have been eliminated. The condensed consolidated financial statements are unaudited and have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP").

The accounting policies followed in the preparation of the interim condensed consolidated financial statements are consistent in all material respects with those presented in Note 2 to the financial statements included on the Annual Report on Form 10-K for the fiscal year ended on December 31, 2016.

Unaudited Interim Financial Information

The condensed consolidated balance sheets at December 31, 2016 was derived from audited financial statements, but does not include all disclosures required by GAAP. The accompanying condensed consolidated balance sheets as of June 30, 2017, the condensed consolidated statements of operations and comprehensive loss for the six months ended June 30, 2017 and 2016 and the condensed consolidated statement of cash flows for the six months ended June 30, 2017 and 2016 are unaudited. The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the audited annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for the fair statement of the Company's financial position as of June 30, 2017, the results of its operations for the six months ended June 30, 2017 and 2016, and its statement of cash flows for the six months ended June 30, 2017 and 2016. The financial data and other information disclosed in the notes related to the six months ended June 30, 2017 and 2016 are unaudited. The results for the six months ended June 30, 2017 and 2016 are not necessarily indicative of results to be expected for the year ending December 31, 2017, any other interim periods, or any future year or period.

The unaudited interim financial statements of the Company included herein have been prepared pursuant to the rules and regulations of the SEC. Certain information and footnote disclosures normally included in financial statements prepared in accordance with GAAP have been condensed or omitted from this report, as is permitted by such rules and regulations. These unaudited condensed consolidated financial statements should be read in conjunction with the audited financial statements and the notes thereto for the year ended December 31, 2016 included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2016.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates, assumptions and judgments that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the condensed consolidated financial statements, and the reported amounts of revenue and expenses during the reporting periods. Significant estimates, assumptions and judgments reflected in these condensed consolidated financial statements include, but are not limited to, the accrual of research and development expenses, the recognition of revenue from the Company's collaboration with Bayer, the valuation of common stock prior to the IPO and the valuation of stock-based awards. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Actual results could differ from the Company's estimates.

Recently Issued Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2014-09, *Revenue from Contracts with Customers (Topic 606)* ("ASU 2014-09"), which supersedes existing revenue recognition guidance under GAAP. The standard's core principle is that a company will recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the Company expects to be entitled in exchange for those goods or services. The standard defines a five-step process to achieve this principle, and will require companies to use more judgment and make more estimates than under the current guidance. The guidance was originally effective for public entities for interim and annual periods beginning after December 15, 2016 and allows for adoption using a full retrospective method, or a modified retrospective method. Early adoption was originally not permitted. In August 2015, the FASB issued ASU 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date*, which delayed the effective date for public entities to annual periods beginning after December 15, 2017 and for interim periods within those fiscal years. Early adoption of the standard is permitted for annual periods beginning after December 15, 2016. In March 2016, the FASB issued ASU 2016-08, *Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations*, to clarify the implementation guidance on principal versus agent considerations. In April 2016, the FASB issued ASU 2016-10, *Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing*, to clarify various aspects of Topic 606, including the identification of performance obligations and the implementation of licensing guidance. The Company is currently evaluating the impact that the adoption of ASU 2014-010 will have on its condensed consolidated financial statements. In May 2016, the FASB issued ASU 2016-12, *Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients,* to clarify aspects of Topic 606, including assessing the collectability criterion, presentation of sales taxes and other similar taxes collected from customers, noncash consideration, contract modifications at transition and completed contracts at transition. The Company is in the process of evaluating the impact of this new guidance.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842)*, which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e. lessees and lessors). The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight line basis over the term of the lease, respectively. A lessee is also required to record a

right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases today. ASC 842 supersedes the previous leases standard, ASC 840 Leases. The standard is effective for public entities for annual and interim periods beginning after December 15, 2018, with early adoption permitted. The Company is in the process of evaluating the impact of this new guidance.

In March 2016, the FASB issued ASU 2016-09, *Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting*, which is intended to simplify several aspects of the accounting for share-based payment awards including income tax consequences, classification of awards as either equity or liabilities and classification within the statement of cash flows. The standard is effective for public entities for annual and interim periods beginning after December 15, 2016. The Company adopted ASU 2016-09 during the quarter January 1, 2017, at which time it changed its accounting policy to account for forfeitures as they occur. The change was applied on a modified retrospective basis and did not have a material impact on the Company's condensed consolidated financial statements and related disclosures.

In March 2017 the FASB issued ASU No. 2017-08, *Receivables - Nonrefundable Fees and Other Costs (Subtopic 310-20): Premium Amortization on Purchased Callable Debt Securities.* This new standard amends the amortization period for certain purchased callable debt securities held at a premium by shortening the amortization period for the premium to the earliest call date. The new standard will be effective for us on January 1, 2019. The Company is in the process of evaluating the impact of this new guidance.

In May 2017, the FASB issued ASU No. 2017-09, Compensation—Stock Compensation (Topic 718) — Scope of Modification Accounting. ASU 2017-09 applies to entities that change the terms or conditions of a share-based payment award. The amendments in ASU 2017-09 include guidance on determining changes to the terms and conditions of share-based payment awards require an entity to apply modification accounting under Topic 718 unless all of the following conditions are met: (1) the fair value of the modified award is the same as the fair value of the original award immediately before the original award is modified. If the modification does not affect any of the inputs to the valuation technique that the entity uses to value the award, the entity is not required to estimate the value immediately before and after the modification; (2) the vesting conditions of the modified award are the same as the vesting conditions of the original award immediately before the original award is modified; and (3) the classification of the modified award as an equity instrument or a liability instrument is the same as the classification of the original award immediately before the original award is modified. The amendments are effective for annual periods, and interim periods within those annual periods, beginning after December 15, 2017 and should be applied prospectively to an award modified on or after the adoption date. The Company is evaluating the impact the amendments will have on our financial positions and results of operations.

3. Fair Value Measurements and Marketable Securities

Fair Value Measurements

The Company's cash equivalents are generally classified within Level 1 of the fair value hierarchy. The Company's investments in marketable securities are classified within Level 2 of the fair value hierarchy.

The fair values of the Company's marketable securities are generally based on prices obtained from independent pricing sources. Consistent with the fair value hierarchy described above, securities with validated quotes from pricing services are generally reflected within Level 2, as they are primarily based on observable pricing for similar assets and/or other market observable inputs. Typical inputs used by these pricing services include, but are not limited to, reported trades, benchmark yields, issuer spreads, bids, offers and/or estimates cash flow, prepayment spreads and default rates.

The following tables present information about the Company's financial assets measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values:

	Fair Value Measurements as of June 30, 2017 using:			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 22,563	$ —	$ —	$ 22,563
Commercial paper	—	2,499	—	2,499
Total cash equivalents	22,563	2,499	—	25,062
Marketable securities:				
Corporate bonds	—	11,210	—	11,210
U.S. government securities	—	11,218	—	11,218
Total marketable securities	—	22,428	—	22,428
Total cash equivalents and marketable securities	$ 22,563	$ 24,927	$ —	$ 47,490

	Fair Value Measurements as of December 31, 2016			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 22,988	$ —	$ —	$ 22,988
U.S. government securities	—	7,246	—	7,246
Total cash equivalents	22,988	7,246	—	30,234
Marketable securities:				
Commercial paper	—	15,814	—	15,814
Corporate Bonds	—	13,671	—	13,671
U.S. government securities	—	18,230	—	18,230
Total marketable securities	—	47,715	—	47,715
Total cash equivalents and marketable securities	$ 22,988	$ 54,961	$ —	$ 77,949

During the six months ended June 30, 2017 and the year ended December 31, 2016, there were no transfers between Level 1 and Level 2.

The carrying amounts reflected in the condensed consolidated balance sheets for accounts payable and accrued expenses approximate fair value due to their short-term maturities. The carrying value of the Company's outstanding notes payable approximates fair value (a Level 2 fair value measurement), reflecting interest rates currently available to the Company.

Marketable Securities

The following tables summarize the Company's marketable securities as of June 30, 2017 and December 31, 2016:

	Fair Value Measurements as of June 30, 2017 using:			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Loss	Fair Value
Assets:				
Corporate Bonds (due within 1 year)	$ 11,222	$ —	$ (12)	$ 11,210
U.S. government securities (due within 1 year)	11,254	—	(36)	11,218
	$ 22,476	$ —	$ (48)	$ 22,428

	Fair Value Measurements as of December 31, 2016 using:			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Loss	Fair Value
Assets:				
Commercial paper (due within 1 year)	$ 15,814	$ —	$ —	$ 15,814
Corporate Bonds (due within 1 year)	9,182	—	(10)	9,172
U.S. government securities (due within 1 year)	7,002	—	—	7,002
Corporate Bonds (due after 1 year through 2 years)	4,512	—	(12)	4,500
U.S. government securities (due after 1 year through 2 years)	11,256	—	(29)	11,227
	$ 47,766	$ —	$ (51)	$ 47,715

4. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

	June 30, 2017	December 31, 2016
External research and development services	$ 2,461	$ 4,409
Payroll and payroll related costs	17	2,234
Restructuring costs	258	—
Professional services	410	433
Other	193	171
	$ 3,339	$ 7,247

5. Notes Payable

On April 18, 2017, the Company borrowed $276 under the Second Amendment to the loan and security agreement with SVB. No additional issuance costs were accrued. In accordance with the terms of the Second Amendment, the borrowed loan amount accrues interest at an annual rate of 3.5%. Under the loan and security agreement we are obligated to make six monthly, interest-only payments related to the borrowed amount. Thereafter, we are obligated to pay 36 monthly installments of interest and principal. In addition, a final payment equal to 6% of the original principal amount is due on the earlier of the maturity date of the advance, acceleration of the terms of the loan, prepayment of the advance or termination of the loan and security agreement.

Through June 30, 2017, we had borrowed a total of $7,827 available under the loan and security agreement, as amended. During the six months ended June 30, 2017, we made $1,120 of scheduled principal repayments. In addition, the Company accrues the related total final payments due of $365 to outstanding debt by charges to interest expense using the effective-interest method from the date of issuance through the maturity date. The effective interest rate of the outstanding debt under the Second Amendment is approximately 6.3%.

As of June 30, 2017 and December 31, 2016, notes payable consist of the following:

	June 30, 2017	December 31, 2016
Notes payable	$ 5,634	$ 6,478
Less: current portion	(2,455)	(2,361)
Notes payable, net of current portion	3,179	4,117
Debt discount, net of accretion	(20)	(30)
Accretion related to final payment	162	82
Notes payable, net of discount, long term	$ 3,321	$ 4,169

Estimated future principal payments due under the loan and security agreement with Silicon Valley Bank ("SVB") as of June 30, 2017 are as follows:

2017 (remainder of year)	$	1,275
2018		2,215
2019		1,929
2020		215
Total	$	5,634

During the three months ended June 30, 2017 and 2016, the Company recognized $73 and $45, respectively, of interest expense related to the loan and security agreement with SVB. During the six months ended June 30, 2017 and 2016, the Company recognized $188 and $66, respectively, of interest expense related to the loan and security agreement with SVB.

6. Collaboration and License Agreements

Bayer HealthCare LLC

In June 2014, we entered into an agreement with Bayer to research, develop and commercialize AAV gene therapy products for treatment of hemophilia A. The research term of the agreement is 54 months. Under this agreement, Bayer has been granted an exclusive license to develop and commercialize one or more novel gene therapies for hemophilia A. We are responsible for the development of DTX201 under the agreement through a proof-of-concept clinical trial, with full reimbursement from Bayer for all project costs in accordance with the mutually agreed upon research budget. Bayer is responsible operationally and will incur the costs of the conduct of the proof-of-concept clinical trial. Upon the successful demonstration of clinical proof of concept, the agreement requires that Bayer use commercially reasonable efforts to manage and fund 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.

Financial Terms

Under the terms of the agreement with Bayer, the Company received a nonrefundable, noncreditable upfront license payment of $20,000 in June 2014 and is eligible to receive development and commercialization milestone payments of up to $232,000, as well as tiered royalty payments ranging in the high single-digit to low double-digit percentages, not exceeding the mid-teens, of net sales of commercialized products resulting from the collaboration, as defined in the agreement with Bayer. Bayer will fund certain research and development services performed by the Company during the research term and will reimburse the Company for all project costs, including any third-party costs, in the performance of its obligations under the annual research plan and in accordance with the mutually agreed upon research budget.

The Company determined that the deliverables under its agreement with Bayer include (i) research services to be provided over the research term, (ii) a development and commercialization license and (iii) the Company's participation in a Joint Steering Committee ("JSC") and a Joint Research and Development Committee ("JRDC") to be provided over the research term. The Company determined that the development and commercialization license and involvement in the JSC and the JRDC do not have standalone value to Bayer and, therefore, are not separable from the delivery of the research services. Therefore, all deliverables under the agreement have been combined and accounted for as a single unit of accounting. Accordingly, the upfront license payment and research payments are being recognized by the Company as revenue on a straight-line basis over the estimated performance period, which approximates the 54-month research term of the agreement with Bayer that commenced in June 2014. As future research payments are earned, the Company will recognize as revenue the portion of payments equal to the percentage of the elapsed research term to the total estimated research term, with the remaining portion of consideration received being recognized over the remaining estimated performance period on a straight-line basis. The Company concluded at the outset of the arrangement that none of the future milestone payments included in the arrangement qualified as substantive milestones. Any future milestone payments will be recognized, along with the other arrangement consideration, over the remaining estimated period of performance, if any, beginning at the time a milestone payment is earned, with a cumulative catch-up being recognized for the elapsed portion of the estimated research term. As of June 30, 2017, the Company had not earned any milestone or royalty payments.

Revenue recognized under the collaboration agreement with Bayer consisted of the following:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
Revenue:				
Bayer Collaboration	$ 4,369	$ 2,371	$ 7,987	$ 4,577
	$ 4,369	$ 2,371	$ 7,987	$ 4,577

During the three and six months ended June 30, 2017 and 2016, research payments earned by the Company under the collaboration agreement totaled $3,097, $5,462, $1,319 and $2,584, respectively. As of June 30, 2017, the unbilled amount of earned research payments was $3,097. The costs incurred by the Company related to the research activities of the collaboration agreement are recorded as research and development expense in the condensed consolidated statements of operations and comprehensive loss.

As of June 30, 2017 and December 31, 2016, deferred revenue related to the collaboration agreement with Bayer totaled $17,252 and $17,326, respectively, which related to the upfront license payment, research services payments and advance payments for future research services.

Term and Termination

The agreement with Bayer expires on a licensed treatment-by-licensed treatment and country-by-country basis until the later of ten years from the date of first commercial sale or when patent claims have expired, lapsed, been abandoned or been invalidated in such country. The Company and Bayer, through the JSC, may mutually agree to terminate the collaboration early in the event clinical development is ended as required by a regulatory authority or in light of data from any studies conducted prior the POC trial. Bayer has the unilateral right to terminate the agreement in its entirety or with respect to one or more country by providing written notice to the Company. Bayer may also terminate the agreement with notice after two unsuccessful attempts to demonstrate clinical POC in a Phase I human POC trial. Bayer may further terminate the agreement with notice in the event that, following the POC trial, there is a material safety issue with respect to a licensed product. Reciprocal termination rights under the agreement include termination for breach and termination for bankruptcy.

7. Stock-Based Compensation

2015 Stock Option and Incentive Plan

In September 2015, the Company's stockholders approved the 2015 Stock Option and Incentive Plan (the "2015 Plan"). The 2015 Plan provides for the grant of incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock units, restricted stock awards, performance share awards, cash-based awards and other stock-based awards. The 2015 Stock Option Plan replaced the Company's 2013 Stock Option and Grant Plan (the "2013 Plan"). The Company will grant no future stock options or other awards under the 2013 Stock Option Plan. Any options or awards outstanding under the 2013 Stock Option Plan remained outstanding and effective.

As of June 30, 2017, the total number of shares reserved under the 2015 Plan and the 2013 Stock Option Plan was 6,890,841 and the Company had 1,415,450 shares available for future issuance under the 2015 Stock Option Plan.

During the three and six months ended June 30, 2017, the Company granted to employees and directors no shares of restricted common stock and options to purchase 88,000 and 1,096,300 shares of common stock.

During the six months ended June 30, 2017, the Company did not grant to non-employees any stock-based awards.

2015 Employee Stock Purchase Plan

As of June 30, 2017, the total number of shares reserved and available under the 2015 Employee Stock Purchase Plan ("ESPP") was 507,020. As of June 30, 2017, there was no activity under the ESPP.

Stock Options

The following table summarizes the Company's stock option activity since December 31, 2016:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2016	4,185,699	$ 4.26	8.4	$ 4,757
Granted	1,096,300	$ 1.94		
Exercised	—	—		—
Cancelled	(231,286)	$ 6.75		
Outstanding as of June 30, 2017	5,050,713	$ 3.64	8.0	$ 984
Options vested and expected to vest as of June 30, 2017	5,050,713	$ 3.64	8.0	$ 984
Options exercisable as of June 30, 2017	2,368,406	$ 3.55	7.2	$ 703

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock at June 30, 2017.

The weighted average grant-date fair value of stock options granted during the three and six months ended June 30, 2017, was $1.17 and $1.94 per share.

Restricted Common Stock

The Company has granted restricted common stock with time-based vesting conditions. Unvested shares of restricted common stock may not be sold or transferred by the holder. These restrictions lapse according to the time-based vesting conditions of each award. The following table summarizes the Company's restricted common stock activity:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested restricted common stock at December 31, 2016	70,053	$ 0.88
Issued	—	
Vested	(41,584)	$ 0.85
Unvested restricted common stock at June 30, 2017	28,469	$ 0.92

The total fair value of restricted common stock vested during the six months ended June 30, 2017 was $60.

Stock-Based Compensation

Stock-based compensation expense related to stock options and restricted common stock was classified in the condensed consolidated statements of operations and comprehensive loss excluding expense associated with stock options modified in connection with the Company's June 2017 restructuring (Refer to Note 10) as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
Research and development	$ 282	$ 267	$ 662	$ 484
General and administrative	582	530	1,242	846
	$ 864	$ 797	$ 1,904	$ 1,330

As of June 30, 2017, total unrecognized compensation cost related to the unvested awards was $6,549, which is expected to be recognized over a weighted average period of 2.39 years.

8. Net Loss per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
Numerator:				
Net loss	$ (12,309)	$ (12,099)	$ (25,801)	$ (21,610)
Denominator:				
Weighted average common shares outstanding — basic and diluted	25,043,962	25,023,731	25,043,506	25,020,443
Less: Weighted average shares of unvested restricted common stock outstanding	(41,430)	(124,252)	(51,344)	(134,620)
Weighted average common shares outstanding used in calculating net loss per share attributable to common stockholders — basic and diluted	25,002,532	24,899,479	24,992,162	24,885,823
Net loss per share attributable to common stockholders — basic and diluted	$ (0.49)	$ (0.49)	$ (1.03)	$ (0.87)

The Company's potential dilutive securities, which include stock options and unvested restricted common stock, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders are the same. The Company excluded the following potential common shares, presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an antidilutive effect:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
Options to purchase common stock	5,050,713	4,148,924	5,050,713	4,148,924
Unvested restricted common stock	28,469	111,635	28,469	111,635
	5,079,182	4,260,559	5,079,182	4,260,559

9. Commitments and Contingencies

Leases

On May 2, 2017, the Company entered into a second amendment to the lease agreement with Rivertech Associates II, LLC for its existing laboratory and office space located at 840 Memorial Drive, Cambridge, Massachusetts. That lease was to expire in January 2018. As amended, the lease will continue for a term of two years through January 2020 with an option to further extend the lease for five additional years. As amended, required lease payments include base rent of $80 per month through January 2019, which increases to $82 per month over the course of the amended lease through January 2020.

The Company also leases office and laboratory space under an operating lease agreement for its Woburn, MA location with a term expiring March 2021 and an option to extend the lease for five additional years.

During the three and six months ended June 30, 2017 and 2016, the Company recognized $302, $566, $263 and $434 of rental expense related to office and laboratory space, respectively.

The following table summarizes the future minimum lease payments under the Cambridge and Woburn operating leases as of June 30, 2017:

Year Ending December 31,		
2017 (remainder of year)	$	607
2018		1,426
2019		1,490
2020		605
2021		132
Total	$	4,260

The Company is further responsible for its pro rata share of operating expenses, real estate taxes and utilities of the facilities housing the leased office and laboratory space.

Legal Proceedings

The Company is not currently party to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company expenses as incurred the costs related to its legal proceedings.

Clinical Trials

On May 10, 2017, the Company announced its decision to discontinue the development of DTX101. The Company will maintain the ongoing DTX101 extension study which will monitor all patients dosed in the recently discontinued Phase 1/2 clinical trial for up to five years post dosing. Related costs will continue to be expensed as incurred.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and certain executive officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company is not aware of any claims under indemnification arrangements, and it has not accrued any liabilities related to such obligations in its condensed consolidated financial statements as of June 30, 2017.

10. Restructuring

On June 27, 2017, the Company announced that it completed a strategic review to focus internal efforts on the advancement of three programs to key clinical milestones. As part of a strategic restructuring, the Company expects to realize savings in operating expenses, including personnel costs, as a result of streamlining headcount by approximately 25% by the end of 2017. These actions are expected to enable the Company to focus on the timely development of gene therapies addressing unmet needs for patients suffering from inherited metabolic diseases.

During the three and six months ended June 30, 2017, the Company recorded $266 of restructuring-related costs in operating expense, including employee severance, benefits and related costs, as well as a stock option modification. The stock option modification is a one-time, non-cash expense of $28. The Company does not expect to incur any additional significant costs associated with this restructuring.

The following table summarizes the restructuring costs by category for the periods indicated:

	Three and Six Months Ended June 30, 2017		
	Cash	Non-Cash	Total
Research and development	$ 199	$ 28	$ 227
General and administrative	67	—	67
	$ 266	$ 28	$ 294

The following table summarizes the restructuring reserve for the periods indicated:

	Three and Six Months Ended June 30, 2017
Restructuring reserve beginning balance	$ —
Restructuring expenses incurred during the period	266
Amounts paid during the period	(8)
Restructuring reserve ending balance	$ 258

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

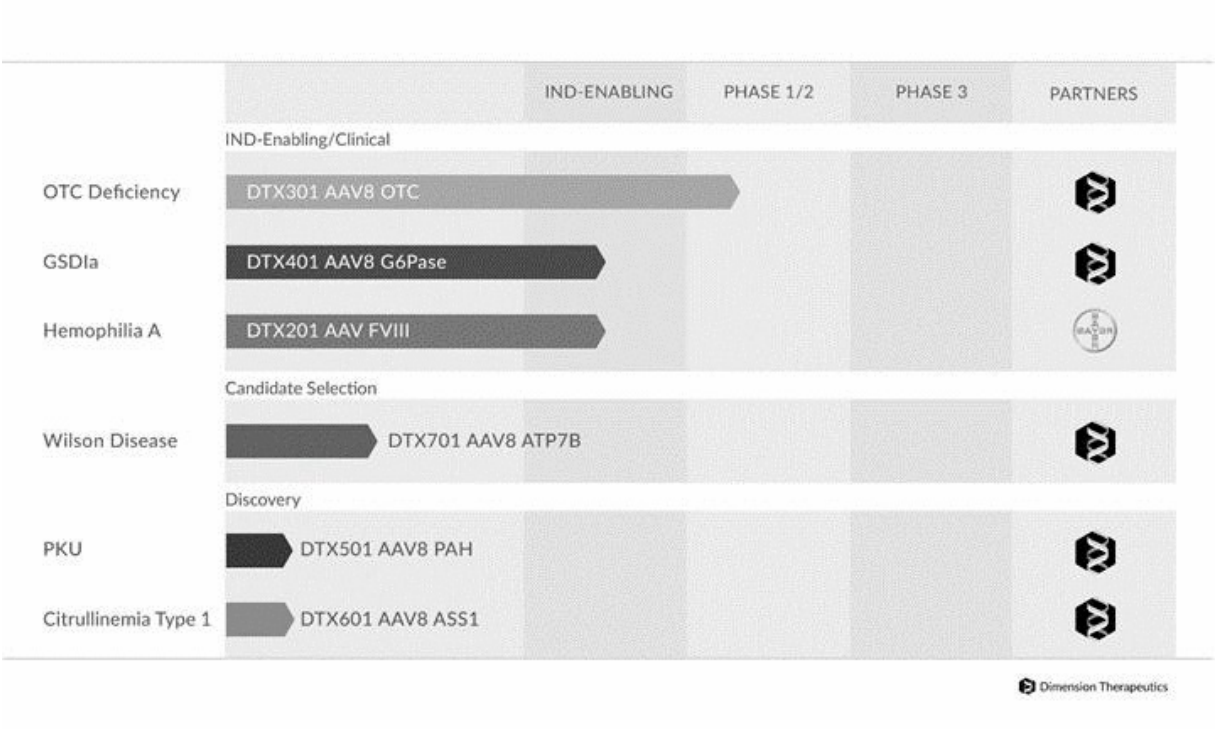
The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our unaudited condensed consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q ("Quarterly Report") and the Annual Report on Form 10-K ("Annual Report") and the audited financial statements and the notes thereto. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business, includes forward looking statements that involve risks and uncertainties. The following information and any forward-looking statements should be considered in light of factors discussed elsewhere in this Quarterly Report on Form 10-Q, including those risks identified under the Risk Factors section. We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made.

Our actual results and timing of certain events may differ materially from the results discussed, projected, anticipated, or indicated in any forward-looking statements. We caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this Quarterly Report on Form 10-Q. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this Quarterly Report on Form 10-Q, they may not be predictive of results or developments in future periods. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made.

Overview

We are a leader in discovering and developing new therapeutic products for people living with devastating rare and metabolic diseases associated with the liver, based on the most advanced mammalian adeno-associated virus (AAV) gene delivery technology. The liver is a vital organ that plays an important role in human metabolism and key physiologic functions, and is the target organ for our programs: ornithine transcarbamylase (OTC) deficiency, glycogen storage disease type Ia (GSDIa), hemophilia A, and Wilson disease. We continue to advance our lead clinical program in OTC deficiency and our preclinical programs, and we retain the global rights to all of our AAV8-based liver-directed programs, with the exception of our hemophilia A program, which is partnered with Bayer. We have developed a robust scientific platform that brings together deep expertise in rare genetic diseases, liver biology, AAV gene therapy, pharmaceutical development, and mammalian vector manufacturing. We believe our continued development of our manufacturing processes, methods and expertise will yield the most comprehensive and leading manufacturing platform developed to date, including our next generation HeLa 2.0 platform, for AAV-based gene therapy product candidates. We believe that by leveraging the expertise created by our platform we will be able to accelerate the research and development of our pipeline of programs while continuing to discover and develop the next generation of products in this field.

Although we discontinued DTX101 for hemophilia B clinical development in May 2017 and announced the completion of our strategic review of corporate priorities in June 2017, described below under the heading "Recent Development," we continue to make progress across our portfolio, including our ongoing Phase 1/2 open-label clinical trial of DTX301 (AAV8 OTC) in OTC deficiency and our IND enabling activities for DTX401 (AAV8 G6Pase) in GSDIa and DTX201 in hemophilia A, the latter in partnership with Bayer. While we remain focused on the advancement and commercialization of AAV gene therapy products for people living with devastating rare and metabolic diseases associated with the liver, following our strategic review, we will focus our internal efforts on the advancement of three programs to key clinical milestones, DTX301 for OTC deficiency, DTX401 for GSDIa and DTX201 for hemophilia A, the latter in partnership with Bayer. Our pipeline consists of the following programs for the treatment of rare and metabolic diseases associated with the liver, also known as inherited metabolic disorders (IMD), and hemophilia:



- **DTX301** is our AAV8 gene therapy product candidate designed for the treatment of patients with OTC deficiency. OTC deficiency is the most common urea cycle disorder and we estimate that there are approximately 10,000 patients worldwide with OTC deficiency, of which we estimate approximately 80% are classified as late-onset, our target population. In November 2016, we submitted an IND for DTX301 with FDA, and in December 2016, we received notification allowing us to proceed with our Phase 1/2 open-label clinical trial of DTX301 and initiated the clinical trial. We have ten sites open in the United States, Canada, Spain and the United Kingdom, and expect to disclose initial data from our Phase 1/2 open-label clinical trial at the end of 2017. In June 2016, our Phase 1/2 clinical trial protocol for DTX301 received unanimous approval by the National Institutes of Health's Recombinant DNA Advisory Committee (RAC). In addition, DTX301 was granted Orphan Drug Designation in the United States and Europe in January and March 2016, respectively, and received Fast Track designation in the United States in January 2017. To evaluate therapeutic response of DTX301, we plan to measure ammonia levels and other biomarkers, including ^{13}C-acetate, which are established measures of OTC deficiency disease status and hepatocyte (liver) ureagenesis capacity, respectively.
- **DTX401** is our AAV8 gene therapy program for the treatment of patients with 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 and we estimate there are approximately 6,000 patients worldwide. We initiated IND-enabling activities in 2016 to support an IND filing for DTX401 by early 2018 and expect initial clinical data from the trial mid-2018. In addition, DTX401 was granted Orphan Drug Designation in the United States and Europe in October and November 2016, respectively. To evaluate the therapeutic response to DTX401, we plan to measure fasting glucose, which is a well-established measure of GSDIa disease status.

- **DTX201** is our FVIII gene therapy program for the treatment of hemophilia A that we are developing in collaboration with Bayer, a global leader in the development and commercialization of innovative therapeutics for treating patients with hemophilia. We are responsible for the development of DTX201 under the agreement through a proof-of-concept clinical trial including all activities associated with process development and manufacturing, with reimbursement from Bayer for all project costs in accordance with the mutually agreed upon research budget. Bayer is responsible operationally and will incur the costs of the conduct of the proof-of-concept clinical trial. Upon the successful demonstration of clinical proof of concept, the agreement requires that Bayer use commercially reasonable efforts to manage and fund 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. We also received an upfront payment of $20.0 million and are eligible for potential development and commercialization milestone payments of up to $232.0 million, as well as royalties on product sales. The relationship with Bayer brings non-dilutive financial benefits and allows us to leverage Bayer's significant experience in the hemophilia market. Hemophilia A is the most common form of hemophilia with approximately 140,000 patients worldwide. We selected a candidate in 2015 and initiated IND-enabling activities for DTX201 in the first quarter of 2016 to support an IND filing for DTX201 by early 2018. We expect initial data from the trial in moderate/severe to severe hemophilia A in 2018. We significantly progressed the HeLa mammalian cell-based suspension platform for DTX201, locking the lab scale manufacturing process, successfully transferring the upstream process and initiating tech transfer for clinical supply at GMP, or good manufacturing practices, scale at our CMO, or contract manufacturing organization. In May and June 2016, we presented data at ASGCT, or the American Society for Gene and Cell Therapy, and EHA, or the European Hemophilia Association, respectively, demonstrating that the selection and integration of specific product components – including the capsid, enhancer, and promoter – further optimized product performance, including long-term expression of Factor VIII (FVIII). To evaluate the therapeutic response of DTX201, we plan to assess clotting factor levels and annual bleeding rates, which are two well-established measures of hemophilia A disease status.
- **DTX701** is our AAV8 gene therapy program for the treatment of patients with Wilson disease, a disorder that arises from a defect in P-type ATPase (ATP7B), an essential transporting protein that translocates copper to ceruloplasmin for biliary excretion. A common inherited metabolic disorder, we estimate there are more than 50,000 patients worldwide. We initiated preclinical activities in collaboration with the University of Pennsylvania in 2016 to support selection of a development candidate in the first half of 2018. To evaluate the therapeutic response to DTX701, we plan to measure serum and urinary copper levels, which are well-established measures of Wilson disease status.
- **DTX501** is our AAV8 gene therapy program for the treatment of patients with PKU, a disease that arises from a defect in phenylalanine hydroxylase (PAH), an essential enzyme in phenylalanine (Phe) metabolism. Considered one of the most common inherited metabolic disorders, we estimate there are more than 50,000 patients worldwide. To evaluate the therapeutic response to DTX501, we plan to measure serum Phe levels, which is a well-established measure of PKU disease status.
- **DTX601** is our AAV8 gene therapy program for the treatment of patients with citrullinemia type I (also referred to as classic citrullinemia), a disease that arises from a defect in argininosuccinate synthase (ASS), an essential enzyme that catalyzes the synthesis of argininosuccinate from citrulline and aspartate, the third step in the urea cycle. The disease can become evident in the first few days of life or later in childhood, and affects approximately 1 in 57,000 births worldwide. To evaluate the therapeutic response to DTX601, we plan to measure ammonia levels and other biomarkers, including ^{13}C-acetate, which are established measures of citrullinemia type I disease status and hepatocyte (liver) ureagenesis capacity, respectively.
- We intend to focus our research and development on future product candidates and novel or next generation capsids that treat well-understood rare monogenic diseases associated with the liver that we believe are well-suited to our gene therapy platform and can leverage learnings from our current programs. We select our programs based on demonstrated preclinical proof of concept in well-described or validated animal models. We seek to address clear unmet medical need in readily identifiable patient populations for which there are no therapies or where current standards of care only manage symptoms.

Recent Development – Completion of strategic review and updated corporate priorities

On June 27, 2017, we announced the completion of a strategic review and our plan to focus internal efforts on the advancement of three programs to key clinical milestones, DTX301 for OTC deficiency, DTX401 for GSDIa, and DTX201 for hemophilia A. The review followed our May 10, 2017 announcement that we would to discontinue development of DTX101, an investigational AAVrh10 based gene therapy product that was being developed for the treatment of moderate/severe-to-severe hemophilia B. Our decision to discontinue the development of DTX101 followed the review of the emerging DTX101 Phase 1/2 clinical study data and the

conclusion of our management and board of directors that the data would not meet the company's minimum target product profile for continued development or future commercialization. In connection with our reprioritization, we expect a reduction in approximately 25% of our workforce by the end of 2017, including workforce reductions and attrition (See Note 10, "Restructuring," in the accompanying notes to the condensed consolidated financial statements for additional information). As a result, we expect to realize savings in operating expenses once the reprioritization is fully implemented. These actions are expected to enable us to focus on the timely development of gene therapies addressing unmet needs for patients suffering from rare and inherited metabolic diseases.

We have initiated a comprehensive evaluation of the DTX101 data to determine what next steps should be taken on the program. As of the August 3, 2017 cutoff date, all patients in cohort 1 and cohort 2 have normal alanine aminotransferase (ALT) levels. Notably, in patient 3 of cohort 2 ALT levels have returned to normal with no lasting effects of the transient elevation in his liver function tests. While we expect our evaluation to take some time to complete, we plan to present full study findings, including results from the biomarker and immune analyses, at a future scientific conference. We remain committed to the hemophilia community, including our ongoing IND enabling activities for DTX201 in hemophilia A, in collaboration with Bayer, and all ongoing follow-up of the six patients dosed in our Phase 1/2 clinical trial of DTX101 in hemophilia B. This includes our ongoing DTX101 extension study for hemophilia B which will monitor all patients dosed for up to five years post dosing. The FDA's Data and Safety Monitoring Committee for our DTX101 Phase 1/2 study has received regular communications and updates on the study data, including the decision to discontinue clinical development of DTX101.

We do not believe the decision to discontinue development of DTX101 will affect the ongoing Phase 1/2 clinical development of DTX301, an AAV8 based gene therapy, in OTC deficiency, or any of our other investigational AAV therapeutic programs in development. While our IMD programs are testing AAV8 vectors, the DTX101 program utilized an AAVrh10 vector. In December 2016, we presented data demonstrating that selection of capsid, a key component of AAV vectors, can impact product efficiency and, potentially, host immune responses to the vector. Systemic delivery of AAVrh10 in non-human primates resulted in higher levels of gene transfer to the primate liver than with other vectors, such as AAV5 and AAV3b. The data also indicated a difference in the ability to re-dose with AAV3b following initial dosing with AAVrh10 (versus initial dosing with AAV8), suggesting a differential immune response following systemic AAVrh10 administration that may not occur subsequent to systemic AAV8 dosing. We have ongoing studies to explore these data and potential causes for the alanine aminotransferase (ALT) changes in the patients dosed in our Phase 1/2 clinical trial of DTX101, including other immune and non-immune causes.

Since our inception on June 20, 2013, we have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, acquiring and developing product and technology rights, and conducting research and development activities for our product candidates. We do not have any products approved for sale and have not generated any revenue from product sales. We have funded our operations to date with proceeds from the sale of our equity securities and payments received in connection with our collaboration agreement with Bayer, and, to a lesser extent, through borrowings under a loan and security agreement. Through June 30, 2017, we had received net proceeds of $88.8 million from our sales of preferred stock, $64.6 million from our initial public offering, $44.1 million under the collaboration agreement with Bayer, and $7.8 million from borrowings under a loan and security agreement.

Since our inception, we have incurred significant operating losses. Our net losses were $12.3 million, $25.8 million, $12.1 million and $21.6 million for the three and six months ended June 30, 2017 and 2016, respectively. As of June 30, 2017, we had an accumulated deficit of $126.0 million. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We expect our expenses and capital requirements will increase in connection with our ongoing activities, as we:

- pursue the preclinical and clinical development of our programs and product candidates, including DTX301, DTX401, DTX201, and DTX701, and maintain our ongoing DTX101 extension study for hemophilia B which will monitor all patients dosed in our recently discontinued Phase 1/2 clinical trial for up to five years post dosing;
- seek to identify and develop additional product candidates;
- develop and scale up our manufacturing processes and capabilities to support our ongoing preclinical activities and clinical trials of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals for any of our un-partnered product candidates that successfully complete clinical development; and
- develop and expand our sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, for our product candidates for which we obtain marketing approval.

We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for our product candidates. If we obtain regulatory approval for any of our product candidates, we expect to incur significant expenses related to developing our internal commercialization capability to support product sales, marketing and distribution. Further, we expect to continue to incur costs associated with operating as a public company.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our product candidates.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of June 30, 2017, we had cash, cash equivalents and marketable securities of $47.5 million. We believe our existing cash, cash equivalents and marketable securities as of June 30, 2017 and reimbursements and $15 million in milestones to be received in connection with our collaboration agreement with Bayer will enable us to fund our operating expenses and capital expenditure requirements to the end of 2018. Without the milestones, the company would be able to fund operations to mid-2018. See "— Liquidity and Capital Resources."

Components of our Results of Operations

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. All of our revenue to date has been derived from our collaboration agreement with Bayer.

In June 2014, we entered into a research and development collaboration and license agreement with Bayer for the development and commercialization of a gene therapy for the treatment of hemophilia A. Under the terms of our agreement with Bayer, we received a nonrefundable, noncreditable upfront license payment of $20.0 million in June 2014 and we are eligible to receive development and commercialization milestone payments of up to $232.0 million, as well as tiered royalty payments ranging in the high single-digit to low double-digit percentages, not exceeding the mid-teens, of net sales of commercialized products resulting from the collaboration, as defined in our agreement with Bayer. Bayer will fund certain research and development services performed by us during the research term and will reimburse us for all project costs, including any third-party costs, in the performance of our obligations under the annual research plan and in accordance with the mutually agreed upon research budget.

The deliverables under our agreement with Bayer include (1) research services to be provided over the research term, (2) a development and commercialization license and (3) our participation in a Joint Steering Committee, or JSC, and a Joint Research and Development Committee, or JRDC, to be provided over the research term. We determined that the development and commercialization license and involvement in the JSC and the JRDC do not have standalone value to Bayer and, therefore, are not separable from the delivery of the research services. Therefore, all deliverables under the agreement have been combined and accounted for as a single unit of accounting. Accordingly, the upfront license payment and research payments are being recognized by us as revenue on a straight-line basis over the estimated performance period, which approximates the 54-month research term of the agreement with Bayer that commenced in June 2014. As future research payments are earned, we will recognize as revenue the portion of payments equal to the percentage of the elapsed research term to the total estimated research term, with the remaining portion of consideration received being recognized over the remaining estimated performance period on a straight-line basis. We concluded at the outset of the arrangement that none of the future milestone payments included in the arrangement qualified as substantive milestones. Any future milestone payments will be recognized, along with the other arrangement consideration, over the remaining estimated period of performance, if any, beginning at the time a milestone payment is earned, with a cumulative catch-up being recognized for the elapsed portion of the estimated research term. As of June 30, 2017, we had not earned any milestone or royalty payments.

During the three and six months ended June 30, 2017 and 2016, we recognized revenue related to our collaboration agreement with Bayer as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
	(in thousands)		(in thousands)	
Revenue:				
Bayer Collaboration	$ 4,369	$ 2,371	$ 7,987	$ 4,577
	$ 4,369	$ 2,371	$ 7,987	$ 4,577

As of June 30, 2017, the unbilled amount of earned research payments was $3.1 million. As of June 30, 2017, we had short-term and long-term deferred revenue of $9.9 million and $7.4 million, respectively, related to our collaboration agreement with Bayer.

We expect that any future revenue recognized under our collaboration agreement will fluctuate from quarter to quarter as a result of the uncertain timing of future milestone payments and the uncertain quantity of our research services provided from quarter to quarter.

Operating Expenses

Research and Development Expenses

Research and development expenses, which include costs of research services incurred in connection with our collaboration with Bayer, consist primarily of costs incurred in connection with the discovery and development of our product candidates, which include:

- employee-related expenses, including salaries, related benefits, travel and stock-based compensation expense for employees engaged in research and development functions;
- expenses incurred in connection with the preclinical and clinical development of our product candidates, including the sponsored research and option, and collaboration agreements with the University of Pennsylvania and our manufacturing agreements with contract manufacturing organizations, or CMOs, and under agreements with contract research organizations, or CROs;
- facilities costs, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and supplies; and
- payments made under third-party licensing agreements.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our service providers.

Our direct research and development expenses are tracked on a program-by-program basis and consist primarily of external costs such as fees paid to academic collaborators, CMOs, CROs and central laboratories in connection with our preclinical development, process development, manufacturing and clinical development activities. We do not allocate employee costs or facility expenses, including depreciation or other indirect costs, to specific product development programs because these costs are deployed across multiple product development programs and, as such, are not separately classified. We use internal resources primarily to conduct our internal process discovery and development, as well as for managing our preclinical development, process development and clinical development activities. These employees work across multiple development programs and, therefore, we do not track their costs by program.

The table below summarizes our research and development expenses incurred by development program:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
	(in thousands)		(in thousands)	
DTX101	$ 915	$ 1,485	$ 2,091	$ 3,851
DTX201	1,646	175	2,724	535
DTX301	4,412	1,778	6,559	3,089
DTX401	1,500	1,327	4,104	1,546
Other research and development programs	862	1,229	1,494	1,437
Unallocated expenses	4,754	5,246	10,831	9,587
Total research and development expenses	$ 14,089	$ 11,240	$ 27,803	$ 20,045

We expect that our expenses will increase in connection with our planned preclinical manufacturing and clinical development activities in the near term. This includes all ongoing follow-up of the six patients dosed in our recently discontinued Phase 1/2 clinical trial of DTX101 in hemophilia B and our ongoing extension study which will monitor all patients dosed for up to five years post dosing. At this time, we cannot reasonably estimate the costs for completing the preclinical and clinical development of any of our product candidates.

The successful development and commercialization of our product candidates is highly uncertain. This is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- successful completion of preclinical studies, including toxicology studies, biodistribution studies and minimally efficacious dose studies in animals, and where applicable and requested, under FDA's Good Laboratory Practice, or GLP;
- approval of Investigational New Drug applications, or INDs, for our product candidates to commence planned clinical trials or future clinical trials;
- successful enrollment in, and completion of, preclinical studies and clinical trials;
- successful data from our clinical program that supports an acceptable benefit-risk profile of our product candidates in the intended populations;
- successful development, and subsequent clearance or approval, of companion diagnostics for use as screening criteria for potential patients;
- receipt of regulatory approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers for clinical supply and commercial manufacturing and, where applicable, commercial manufacturing capabilities;
- successful development of our internal manufacturing processes and transfer to larger-scale facilities operated by either a CMO, or by us;
- establishment and maintenance of patent and trade secret protection or regulatory exclusivity for our product candidates;
- commercial launch of our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of the product candidates, if and when approved, by patients, the medical community and third-party payors;
- effective competition with other therapies;
- establishment and maintenance of healthcare coverage and adequate reimbursement;
- enforcement and defense of intellectual property rights and claims; and
- maintenance of a continued acceptable safety profile of the product candidates following approval.

Any changes in the outcome of any of these variables with respect to the development of our product candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs, including stock-based compensation, for personnel in executive, finance and administrative functions. General and administrative expenses also include direct and allocated facility-related costs, as well as professional fees for legal, patent, consulting, accounting and audit services.

Interest Income (Expense), net

Interest income (expense), net consists of interest earned on our cash, cash equivalents and marketable securities, as well as interest expense incurred on borrowings at various dates under our loan and security agreement entered into in August 2014, as amended.

Critical Accounting Policies and Significant Judgments and Estimates

The accounting policies followed in the preparation of our interim condensed consolidated financial statements appearing at the beginning of this Quarterly Report on Form 10-Q are consistent in all material respects with those included in the Company's Annual Report on the Form 10-K for the fiscal year ended on December 31, 2016 and Note 2 in our condensed consolidated unaudited financial statements included in this Quarterly Report on Form 10-Q.

Results of Operations

Comparison of the Three Months Ended June 30, 2017 and 2016

The following table summarizes our results of operations for the three months ended June 30, 2017 and 2016:

	Three Months Ended June 30,		Increase
	2017	2016	(Decrease)
	(in thousands)		
Revenue	$ 4,369	$ 2,371	$ 1,998
Operating expenses:			
Research and development	14,089	11,240	2,849
General and administrative	2,610	3,236	(626)
Total operating expenses	16,699	14,476	2,223
Loss from operations	(12,330)	(12,105)	(225)
Interest income (expense), net	21	6	15
Net loss	$ (12,309)	$ (12,099)	$ (210)

Revenue

We generate revenue from our collaboration agreement with Bayer and recognized $4.4 million of revenue for the three months ended June 30, 2017 and $2.4 million for three months ended June 30, 2016. The $2.0 million increase was due to services performed in connection with our performance obligations under the collaboration agreement with Bayer. Amounts recorded as deferred revenue under the collaboration agreement with Bayer totaled $17.3 million as of June 30, 2017 and $17.3 million as of December 31, 2016.

Research and Development Expenses

	Three Months Ended June 30,		Increase
	2017	2016	(Decrease)
	(in thousands)		
Direct research and development expenses by program:			
DTX101	$ 915	$ 1,485	$ (570)
DTX201	1,646	175	1,471
DTX301	4,412	1,778	2,634
DTX401	1,500	1,327	173
Other research and development programs	862	1,229	(367)
Unallocated research and development expenses:			
Personnel related (including stock-based compensation)	2,411	2,513	(102)
Services	524	649	(125)
Facility related	545	492	53
Lab consumables and other	1,274	1,592	(318)
Total research and development expenses	$ 14,089	$ 11,240	$ 2,849

Research and development expenses were $14.1 million for the three months ended June 30, 2017, compared to $11.2 million for the three months ended June 30, 2016. The increase of $2.9 million was due primarily to the increase of $2.6 million in DTX301 manufacturing and clinical expenses as we transition from preclinical development to our Phase 1/2 clinical trial, and $1.5 million in DTX201 manufacturing and IND-enabling expenses, offset by a decrease of $0.6 million DTX101-related expenses due to lower clinical and manufacturing expenses and $0.9 million of other research and development programs and unallocated research and development expenses.

General and Administrative Expenses

	Three Months Ended June 30,		Increase
	2017	2016	(Decrease)
	(in thousands)		
Personnel related (including stock-based compensation)	$ 1,270	$ 1,628	$ (358)
Professional fees	1,026	1,166	(140)
Facility related	156	184	(28)
Other	158	258	(100)
Total general and administrative expenses	$ 2,610	$ 3,236	$ (626)

General and administrative expenses were $2.6 million for the three months ended June 30, 2017, compared to $3.2 million for the three months ended June 30, 2016. The decrease of $0.6 million was primarily due to a $0.4 million decrease in personnel related costs.

Interest Income (Expense), net

Our interest income (expense), net consisted of interest earned on our cash equivalents and marketable securities as well as interest expense incurred on borrowings at various dates under our loan and security agreement entered into with SVB in August 2014, as last amended in February 2016. We recorded $21 thousand of interest income, net of $119 thousand of interest expense, for the three months ended June 30, 2017, compared to $6 thousand of interest income, net of $45 thousand of interest expense, for the three months ended June 30, 2016.

Comparison of the Six Months Ended June 30, 2017 and 2016

The following table summarizes our results of operations for the six months ended June 30, 2017 and 2016:

	Six Months Ended June 30,		Increase
	2017	2016	(Decrease)
	(in thousands)		
Revenue	$ 7,987	$ 4,577	$ 3,410
Operating expenses:			
Research and development	27,803	20,045	7,758
General and administrative	6,042	6,177	(135)
Total operating expenses	33,845	26,222	7,623
Loss from operations	(25,858)	(21,645)	(4,213)
Interest income (expense), net	57	35	22
Net loss	$ (25,801)	$ (21,610)	$ (4,191)

Revenue

We generate revenue from our collaboration agreement with Bayer and recognized $8.0 million of revenue for the six months ended June 30, 2017 and $4.6 million for the six months ended June 30, 2016. The $3.4 million increase was due to services performed in connection with our performance obligations under the collaboration agreement with Bayer. Amounts recorded as deferred revenue under the collaboration agreement with Bayer totaled $17.3 million and $17.3 million as of June 30, 2017 and 2016, respectively.

Research and Development Expenses

	Six Months Ended June 30,		Increase
	2017	2016	(Decrease)
	(in thousands)		
Direct research and development expenses by program:			
DTX101	$ 2,091	$ 3,851	$ (1,760)
DTX201	2,724	535	2,189
DTX301	6,559	3,089	3,470
DTX401	4,104	1,546	2,558
Other research and development programs	1,494	1,437	57
Unallocated research and development expenses:			
Personnel related (including stock-based compensation)	5,919	4,743	1,176
Services	1,283	1,399	(116)
Facility related	1,093	777	316
Lab consumables and other	2,536	2,668	(132)
Total research and development expenses	$ 27,803	$ 20,045	$ 7,758

Research and development expenses were $27.8 million for the six months ended June 30, 2017, compared to $20.0 million for the six months ended June 30, 2016. The increase of $7.8 million was due primarily to the increase of $3.5 million in DTX301 manufacturing and clinical expenses as we transition from preclinical development to our Phase 1/2 clinical trial, $2.6 million in DTX401 manufacturing and IND-enabling expenses, $2.2 million in DTX201 manufacturing and IND-enabling expenses, and $1.2 million of unallocated research and development expenses, offset by decrease of $1.8 million in DTX101-related expenses due to lower clinical activity and manufacturing expenses. The increase of $1.2 million in unallocated research and development expenses was due to $1.2 million increase in personnel-related costs (including $0.3 million stock-based compensation) as a result of hiring additional full-time employees to support the growth in our operations.

General and Administrative Expenses

	Six Months Ended June 30,		Increase
	2017	2016	(Decrease)
	(in thousands)		
Personnel related (including stock-based compensation)	$ 3,091	$ 3,048	$ 43
Professional fees	2,230	2,347	(117)
Facility related	306	290	16
Other	415	492	(77)
Total general and administrative expenses	$ 6,042	$ 6,177	$ (135)

General and administrative expenses were $6.0 million for the six months ended June 30, 2017, compared to $6.2 million for the six months ended June 30, 2016.

Interest Income (Expense), net

Our interest income (expense), net consisted of interest earned on our cash equivalents as well as interest expense incurred on borrowings at various dates under our loan and security agreement entered into with SVB in August 2014, as amended. We recorded $57 thousand of interest income, net of $216 thousand of interest expense, for the six months ended June 30, 2017, compared to $35 thousand of interest expense, net of $66 thousand of interest income, for the six months ended June 30, 2016.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We have generated revenue to date only from our collaboration agreement with Bayer. We have not yet commercialized any of our product candidates, which are in various phases of preclinical and clinical development, and we do not expect to generate revenue from sales of any product for several years, if at all. We have funded our operations to date with proceeds from the sale of our equity securities and payments received in connection with our collaboration agreement with Bayer, and, to a lesser extent, through borrowings under a loan and security agreement, as amended, that we entered into with SVB in August 2014. Through June 30, 2017, we had received net proceeds of $88.8 million from our sales of preferred stock, $64.6 million from our IPO, $44.1 million under the collaboration agreement with Bayer, and $7.8 million from borrowings under a loan and security agreement.

As of June 30, 2017, we had cash, cash equivalents and marketable securities totaling $47.5 million. We invest our cash in money market funds, U.S. government securities, corporate bonds, and commercial paper, with the primary objectives to preserve principal, provide liquidity and maximize income without significantly increasing risk.

Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	Six Months Ended June 30,	
	2017	2016
	(in thousands)	
Cash used in operating activities	$ (29,495)	$ (21,326)
Cash provided by (used in) in investing activities	25,227	(4,906)
Cash used in financing activities	(904)	3,836
Net (decrease) increase in cash and cash equivalents	$ (5,172)	$ (22,396)

Operating activities. During the six months ended June 30, 2017, operating activities used $29.5 million of cash, resulting from our net loss of $25.8 million, partially offset by non-cash charges of $3.1 million and cash used by changes in our operating assets and liabilities of $6.8 million. Net cash used by changes in our operating assets and liabilities for the six months ended June 30, 2017 consisted primarily of a $1.2 million increase in accounts receivable, a $0.6 million increase in prepaid expense, $1.0 million decrease in accounts payable, and a $3.9 decrease in accrued expenses.

During the six months ended June 30, 2016, operating activities used $21.3 million of cash, resulting from our net loss of $21.6 million, partially offset by non-cash charges of $2.0 million and cash used by changes in our operating assets and liabilities of $1.7 million. Net cash used by changes in our operating assets and liabilities for the six months ended June 30, 2016 consisted primarily of a $1.2 million decrease in accounts payable. These changes were offset by a $1.2 million decrease in accounts receivable, $1.0 million decrease in prepaid expense and a $1.1 million increase in accrued expense.

Investing activities. During the six months ended June 30, 2017, net cash provided by investing activities $25.2 million of cash in investing activities, consisting primarily of sales and maturities of marketable securities of $25.3 million.

During the six months ended June 30, 2016, we used $4.9 million of cash in investing activities, consisting primarily of purchases of property and equipment related to the Woburn, MA facility.

Financing activities. During the six months ended June 30, 2017, financing activities used $0.9 million, consisting primarily of repayment of notes payable of $1.1 million which were offset by proceeds from issuance of notes payable of $0.3 million.

During the six months ended June 30, 2016, net cash provided by financing activities was $3.8 million, consisting of proceeds from issuance of notes payable of $4.1 million which were offset by repayment of notes payable of $0.3 million.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials of our product candidates in development, including as we:

- pursue the preclinical and clinical development of our most advanced programs and product candidates, including DTX201, DTX301 and DTX401, and maintain our ongoing DTX101 extension study for hemophilia B which will monitor all patients dosed in our recently discontinued Phase 1/2 clinical trial for up to five years post dosing;
- continue the research and development of our other product candidates;
- seek to identify and develop additional product candidates;
- scale up our manufacturing processes and capabilities to support our ongoing preclinical activities and clinical trials of our product candidates and commercialization of any of our product candidates for which we obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- seek marketing approvals for any of our product candidates that successfully complete clinical development; and
- develop and expand our sales, marketing and distribution capabilities for our product candidates for which we obtain marketing approval.

As of June 30, 2017, we had cash, cash equivalents and marketable securities of $47.5 million. We believe our existing cash, cash equivalents and marketable securities as of June 30, 2017 and reimbursements and $15 million in milestones to be received in connection with our collaboration agreement with Bayer will enable us to fund our operating expenses and capital expenditure requirements to the end of 2018. Without the milestones, the company would be able to fund operations to mid-2018. This raises substantial doubt of our ability to operate as a going concern for a period of one year from the issuance of these financial statements. See Note 1 to the condensed consolidated financial statements for management's plans. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect or fail to achieve certain milestones under the Bayer agreement.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical drugs, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements will depend on and could increase significantly as a result of many factors, including:

- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the scope, prioritization and number of our research and development programs;
- the success of our collaboration with Bayer;
- the success of our development, and the subsequent timing and outcome of regulatory clearance or approval, of companion diagnostics for use as screening criteria for potential patients;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we obtain;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of establishing or contracting for manufacturing capabilities if we obtain regulatory clearances to manufacture our product candidates;
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory clearances to market our product candidates; and
- our ability to establish and maintain healthcare coverage and adequate reimbursement.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements or marketing and distribution arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through other third-party funding, collaborations agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Loan and Security Agreement

In August 2014, we entered into a loan and security agreement with Silicon Valley Bank ("SVB"), which provided for advances under an equipment line of up to $1.8 million. Through June 30, 2017, we had borrowed $1.8 million available under the loan and security agreement and had made $1.3 million of scheduled principal repayments. Under the loan and security agreement, for each

advance under the equipment line, we are obligated to make six monthly, interest-only payments. Thereafter, we are obligated to pay 36 monthly installments of interest and principal. Outstanding principal under the loan and security agreement accrue interest at an annual rate of 5.5%, which was determined on the date of each drawdown.

In connection with entering into the loan and security agreement, in August 2014, we granted to the lender a warrant to purchase 11,973 shares of our common stock at an exercise price of $0.56 per share. This warrant was exercised at the option of the lender by the option of a cashless exercise in December 2015 resulting in the issuance of 11,306 of our common shares.

In December 2015, we amended the loan and security agreement with SVB in connection with the formation of our securities corporation. The amendment calls for us and our subsidiaries, excluding our securities corporation, to maintain all operating, depository and securities accounts with SVB, provided, further, we shall have at all times at least 105% of the then-outstanding loan obligations on deposit in operating, depository and securities accounts maintained with SVB.

In February 2016, we entered into a second amendment to the loan and security agreement with SVB. Under the second amendment, we may borrow an aggregate principal amount of up to $7.0 million for certain equipment purchases. Through June 30, 2017, we had borrowed $6.1 million under second amendment of our loan and security agreement and made $0.9 million of scheduled principal payments. Under the loan and security agreement, for each advance under the equipment line, we are obligated to make six monthly, interest-only payments. Thereafter, we are obligated to pay 36 monthly installments of interest and principal. Outstanding principal under the advances of the second amendment to the loan and security agreement accrue interest at an annual rate of 3.0%, which was determined on the date of each drawdown. In addition, the Company is required to make an additional final payment equal to 6% of the original principal amount of each advance due on the earliest to occur of the maturity date of the advance, acceleration of the terms of the loan, prepayment of the advance or termination of the loan and security agreement. As of June 30, 2017, the Company accrues the related total final payments due of $0.4 million to outstanding debt by charges to interest expense using the effective-interest method from the date of issuance through the maturity date.

Through June 30, 2017, we had borrowed a total of $7.8 million available under the loan and security agreement, as amended, and had made $2.2 million of scheduled principal repayments. Borrowings under the loan and security agreement are secured by substantially all of our assets, except for our intellectual property. There are no financial covenants associated with the loan and security agreement. There are negative covenants restricting our activities, such as disposing of our business or certain assets, changing our business, management, ownership or business locations, incurring additional debt or liens or making payments on other debt, making certain investments and declaring dividends, acquiring or merging with another entity, engaging in transactions with affiliates or encumbering intellectual property. The obligations under the loan and security agreement are subject to acceleration upon occurrence of specified events of default, including a material adverse change in our business, operations or financial or other condition.

Contractual Obligations and Commitments

On May 2, 2017, the Company entered into a second amendment to the lease agreement with Rivertech Associates II, LLC for its existing laboratory and office space located at 840 Memorial Drive, Cambridge, Massachusetts. That lease was to expire in January 2018. As amended, the lease will continue for a term of two years through January 2020 with an option to further extend the lease for five additional years. The Company will make annual base rent payments of $0.9 million and $1.0 million in the first and second years, respectively, of the extended lease term. The Company is further responsible for its pro rata share of operating expenses, real estate taxes and utilities of the facilities housing the leased office and laboratory space.

Other than the above, there were no material changes to our contractual obligations and commitments described under Management's Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, as filed with the SEC on March 9, 2017.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the Securities and Exchange Commission.

Recently Issued and Adopted Accounting Pronouncements

We have reviewed all recently issued standards and have determined that, other than as disclosed in Note 2 to our unaudited condensed consolidated financial statements appearing at the beginning of this Quarterly Report on Form 10-Q, such standards will not have a material impact on our condensed consolidated financial statements or do not otherwise apply to our operations.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We had cash, cash equivalents and marketable securities of approximately $47.5 million at June 30, 2017. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. Our primary exposure to market risk relates to fluctuations in interest rates, which are affected by changes in the general level of U.S. interest rates. Given the short-term nature of our cash, cash equivalents and marketable securities and the conservative nature of our investments, we believe that a sudden change in market interest rates would not be expected to have a material impact on our financial condition and/or results of operation. We do not own any foreign currency or other derivative financial instruments.

Item 4. Controls and Procedures.

Management's Evaluation of our Disclosure Controls and Procedures

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) or 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Based on this evaluation, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this report. In designing and evaluating our disclosure controls and procedures, our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of June 30, 2017, our disclosure controls and procedures were effective at the reasonable assurance level.

We continue to review and document our disclosure controls and procedures, including our internal controls and procedures for financial reporting, and may from time to time make changes aimed at enhancing their effectiveness and to ensure that our systems evolve with our business.

Changes in Internal Control Over Financial Reporting

During the three months ended June 30, 2017, there have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Securities Exchange Act of 1934, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

From time to time, we may be involved in lawsuits, claims, investigations and proceedings, consisting of intellectual property, commercial, employment and other matters which arise in the ordinary course of business. We are not currently a party to any material legal proceedings.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the following risks and uncertainties, together with all other information in this Quarterly Report on Form 10-Q, including our condensed consolidated financial statements and related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations", before investing in our common stock. The risk factors set forth below with an asterisk (*) next to the title are new risk factors or risk factors containing material changes from the risk factors previously disclosed in Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2016, as filed with the SEC on March 9, 2017. Any of the risk factors we describe below could adversely affect our business, financial condition or results of operations. The market price of our common stock could decline if one or more of these risks or uncertainties actually occur, causing you to lose all or part of the money you paid to buy our common stock. Additional risks that we currently do not know about or that we currently believe to be immaterial may also impair our business. Certain statements below are forward-looking statements. See "Special Note Regarding Forward-Looking Statements" in this Quarterly Report on Form 10-Q for the six months ended June 30, 2017.

Risks Related to Product Development and Regulatory Approval

We are very early in our development efforts. One product candidate, DTX301 for OTC deficiency, entered Phase 1/2 clinical development in December 2016, and the rest of our product candidates are still in preclinical development. If we are unable to advance our product candidates to and through clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We have invested substantially all of our efforts and financial resources in the identification, clinical and preclinical development of our current and future product candidates, DTX301 for ornithine transcarbamylase, or OTC, deficiency, DTX401 for glycogen storage disease type Ia, or GSDIa, DTX201 for hemophilia A, DTX701 for Wilson disease, and our discovery programs DTX501 for phenylketonuria, or PKU, and DTX601 for citrullinemia type I, as well as our recently discontinued Phase 1/2 clinical trial of DTX101 in hemophilia B. We are very early in our development efforts with one product candidate in Phase 1/2 clinical development and the rest of our product candidates are still in preclinical development. In 2016, we completed product candidate selection for our DTX401 and DTX201 programs. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. We currently generate no revenue from sales of any product and we may never be able to develop or commercialize a marketable product.

Each of our programs and product candidates will require additional preclinical and clinical development, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. In addition, our product development programs must be approved or cleared for marketing by the U.S. Food and Drug Administration, or FDA, or certain other foreign regulatory agencies, including the European Medicines Agency, or the EMA, before we may commercialize our product candidates.

The success of our product candidates will depend on several factors, including the following:

- successful enrollment in, and completion of, preclinical studies and clinical trials;
- successful completion of preclinical studies, including toxicology studies, biodistribution studies and minimally efficacious dose studies in animals, and, where applicable, under FDA's Good Laboratory Practice, or GLP;
- approval of Investigational New Drug applications, or INDs, and Clinical Trial Authorisation, or CTAs, for our product candidates to commence planned clinical trials or future clinical trials;
- successful data from our clinical program that supports an acceptable risk-benefit profile of our product candidates in the intended populations;
- successful development, and subsequent clearance or approval, of companion diagnostics for use as screening criteria for potential patients;

- receipt of regulatory approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers for clinical supply and commercial manufacturing and, where applicable, commercial manufacturing capabilities;
- successful development of our internal manufacturing processes and transfer to larger-scale facilities operated by either a contract manufacturing organization, or CMO, or by us;
- establishment and maintenance of patent and trade secret protection or regulatory exclusivity for our product candidates;
- commercial launch of our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of the product candidates, if and when approved, by patients, the medical community and third-party payors;
- effective competition with other therapies;
- establishment and maintenance of healthcare coverage and adequate reimbursement;
- enforcement and defense of intellectual property rights and claims; and
- maintenance of a continued acceptable safety profile of the product candidates following approval.

If we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

FDA, the NIH, Health Canada, and the EMA have demonstrated caution in their regulation of gene therapy treatments, and ethical and legal concerns about gene therapy and genetic testing may result in additional regulations or restrictions on the development and commercialization of our product candidates, which may be difficult to predict.

The clinical trial requirements of FDA, the NIH, Health Canada, the EMA and other 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. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or more extensively studied product candidates. Only one AAV gene therapy product, Glybera from uniQure N.V., or uniQure, has received marketing authorization from the European Commission and no gene therapy product has yet been approved in the United States. Approvals by the European Commission may not be indicative of what FDA may require for approval and different or additional preclinical studies or clinical trials may be required to support regulatory approval in each respective jurisdiction.

Additionally, FDA, the U.S. National Institutes of Health, or NIH, Health Canada, and the EMA have each expressed interest in further regulating biotechnology, including gene therapy and genetic testing. For example, the EMA 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. Such action may delay or prevent commercialization of some or all of our product candidates. For example, in 1999, a patient suffering from OTC deficiency died during a gene therapy clinical trial that utilized an adenovirus vector. It was discovered, unfortunately, that adenoviruses could generate an extreme immune system reaction that can be life-threatening. Thereafter, in January 2000, FDA halted that trial and began investigating 69 other gene therapy trials underway in the United States. Eventually, 28 trials were reviewed, with 13 requiring remedial action. Subsequently, in 2003, FDA suspended 27 additional gene therapy trials involving several hundred patients after learning that a child treated in France had developed leukemia. Although FDA was not aware of any patients treated in these U.S. trials that had suffered illnesses similar to that of the child in France, it nevertheless took precautions. This temporary halt, the largest such action involving gene therapy trials, was a setback for the field.

Regulatory requirements in the United States and abroad governing gene therapy products have changed frequently and may continue to change in the future. FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research to consolidate the review of gene therapy and related products, and has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise this review. Prior to submitting an IND, our human gene therapy clinical trials are subject to review by the NIH Office of Biotechnology Activities', or OBA's, Recombinant DNA Advisory Committee, or the RAC. As of April 2016, the updated NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, including gene therapy, provide the opportunity for one or more oversight bodies (institutional review board ("IRB") or the institutional biosafety committee ("IBC")) to request a public RAC review based on their own review of the protocol and NIH requirements. Regardless of the request for public review, NIH RAC members make their own assessment as to whether the protocol would significantly benefit from a public RAC review. The RAC's recommendations are shared with FDA and the oversight bodies. The RAC can delay the initiation of a clinical trial, even if FDA has reviewed the trial design and details and has not objected to its

initiation or has notified the sponsor that the study may begin. Conversely, FDA can put an IND on a clinical hold even if the RAC has provided a favorable review or has recommended against an in-depth, public review. Moreover, under guidelines published by the NIH, patient enrollment in our gene therapy clinical trials cannot begin until, among other things, the investigator for that clinical trial has received a letter from the OBA indicating that the protocol registration process has been completed. Upon receipt of the letter from OBA confirming completion of protocol registration the investigator may obtain final approval from the oversight bodies and patient enrollment may begin if all other applicable regulatory authorizations have been obtained.

If there is a public RAC review, the receipt of the final recommendation letter concludes the protocol registration process and then oversight body, or bodies, approval can be issued. While the RAC completed its initial public review for DTX301, approving the protocol and issuing written recommendations, the RAC will continue to review DTX301, and may recommend additional public reviews in the future with respect to DTX301 or any of our other product candidates. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause FDA or other oversight bodies to change the requirements for approval of any of our product candidates. Similarly, the EMA governs the development of gene therapies in the European Union and may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines.

These regulatory review committees and advisory groups and the new guidelines they promulgate 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.

We may never obtain FDA approval for any of our product candidates in the United States, and even if we do, we may never obtain approval for or commercialize any of our product candidates in any other jurisdiction, which would limit our ability to realize their full market potential.

In order to eventually market any of our product candidates in any particular foreign jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a jurisdiction-by-jurisdiction basis regarding safety and efficacy. Approval by FDA in the United States, if obtained, does not ensure approval by regulatory authorities in other countries or jurisdictions. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional preclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. The foreign regulatory approval process involves all of the risks associated with FDA approval. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be unrealized.

If preclinical studies for DTX401 for GSDIa, DTX201 for hemophilia A, DTX701 for Wilson disease, DTX501 for PKU, and DTX601 for citrullinemia type I, or all of our future product candidates do not result in the determination of a minimally effective dose range, we may not obtain the regulatory approvals required to initiate clinical testing.

As with any systemically delivered adeno-associated virus, or AAV, gene therapy, it is important that we accurately determine a minimally effective dose in order to successfully execute our clinical trial. Exposure to the AAV virus has been shown to induce the production of neutralizing antibodies, which can reduce or eliminate the therapeutic effect of subsequently administered intravenous AAV therapies such as our product candidates. Because of the potential for immune response producing neutralizing antibodies making patients ineligible for a second dose of that vector, clinical trials are required to determine the minimum effective dose and the maximum safe dose. If our preclinical studies fail to demonstrate a starting dose in the clinic that might be reasonably expected to result in a clinical benefit, regulatory agencies may not approve the start of our clinical trials. In addition, even if we start our clinical program, we may not be able to recruit patients who will seek assurance of a clinical benefit following administration of our therapy.

Clinical development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We have focused our research and development efforts to date on our ongoing Phase 1/2 open-label clinical trial of DTX301 for OTC deficiency, which was initiated in December 2016, as well as our recently discontinued Phase 1/2 clinical trial of DTX101 in hemophilia B, and on our gene therapy platform, identifying our targeted disease indications and our initial product candidates, and our future success depends on our successful development of viable AAV, gene therapy product candidates. These product candidates are based on a relatively new technology that has been exposed to a limited number of patients in the clinic, which makes it difficult to predict the time and cost of development.

In addition to our Phase 1/2 clinical trial of DTX301, we have initiated, completed, or are completing IND-enabling activities on several of our other programs. Commencing each of these clinical trials is subject to acceptance by FDA of our IND and finalizing the trial design based on discussions with FDA and other regulatory authorities. In the event that FDA requires us to complete additional preclinical studies or we are required to satisfy other FDA requests, the start of subsequent clinical trials of DTX301 or our other product candidates may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence our clinical trials or change their position on the acceptability of our trial designs or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect. Successful completion of our clinical trials is a prerequisite to submitting a biologics license application, or BLA, to FDA and a marketing authorization application, or MAA, to the EMA for each product candidate and, consequently, to obtaining approval and initiating commercial marketing of our current and future product candidates. We do not know whether any of our clinical trials will begin or be completed on schedule, if at all.

We may experience delays in completing our preclinical studies and initiating or completing clinical trials. We also may experience numerous unforeseen events during, or as a result of, any future clinical trials that we conduct that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- governmental regulators, IRBs or ethics committees may not authorize or may delay authorizing us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon drug development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors, who we utilize for screening patients for neutralizing antibodies prior to enrollment in our ongoing Phase 1/2 open-label clinical trial of DTX301, and future clinical trials with DTX401, DTX201, DTX701, DTX501, DTX601, and all future product candidates, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate, including as a result of scientific challenges encountered in connection with transitioning from HEK293 to a HeLa platform, such as process design and scaling issues, or any delays in production of cGMP product for our clinical trials;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs or ethics committees to suspend or terminate the trials, or reports may arise from preclinical or clinical testing of other gene therapies that raise safety or efficacy concerns about our product candidates; or
- FDA or other regulatory authorities may require us to submit additional data or impose other requirements, including relating to the stability, expiry or potency of our product candidates, before permitting us to initiate a clinical trial.

We could encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, the Data Safety Monitoring Board, or DSMB, for such trial or FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects that arise in our trial or that occur in other gene therapy trials utilizing AAV vectors sponsored by third parties, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, FDA may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials. Any delays in our preclinical or future clinical development programs may harm our business, financial condition and prospects significantly.

Our transition from HEK293 to a HeLa platform may require comparability studies, which may result in delays to the approval process for our current or future programs and increased costs resulting from additional preclinical trials.

We have conducted some of our preclinical evaluations with viral vectors produced on adherent and suspension platforms utilizing human embryonic kidney 293, or HEK293, cells. We are conducting our Phase 1/2 trial of DTX301, and plan to conduct our Phase 1/2 trials of DTX401, and potentially other programs using viral vectors produced on the HEK293 platform. For Phase 3 studies and commercial production of each of our product candidates, we plan to use an immortal cell line used in scientific research known as HeLa. HeLa is the oldest and most commonly used human cell line. Even if we successfully complete our planned preclinical studies and clinical trials using vectors produced on our adherent and suspension HEK293 platforms, FDA or other regulatory authorities may require a clinical bridge study, or comparability study, showing comparability of vectors produced on the HeLa platform prior to commencing Phase 3 trials of DTX301, DTX401, DTX701, DTX501, and DTX601 delaying the development process. If we make manufacturing or formulation changes to our product candidates in the future, we may need to conduct additional preclinical studies to bridge our modified product candidates to earlier versions. If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- be subject to post-marketing testing requirements; or
- have the drug removed from the market after obtaining marketing approval.

Our product development costs also will increase if we experience delays in testing or regulatory approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. Any delays in our preclinical or future clinical development programs may harm our business, financial condition and prospects significantly.

We may not be successful in our efforts to use and expand our development platform to build a pipeline of product candidates.

A key element of our strategy is to use our targeted focus, premiere execution and team of leading experts, to identify genetically defined diseases with high unmet medical need in order to build a pipeline of product candidates. Although our research and development efforts to date have resulted in a pipeline of product candidates, we may not be able to continue to identify and develop new product candidates. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development. For example, they may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our approach, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price. There is no assurance that our platform will successfully accelerate our preclinical and clinical development, and the process of obtaining regulatory approvals will, in any event, require the expenditure of substantial time and financial resources.

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize, or will be delayed in commercializing, our product candidates and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export are subject to comprehensive regulation by FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Before we can commercialize any of our product candidates, we must obtain marketing approval. We have not received approval or clearance to market any of our product candidates from regulatory authorities in any jurisdiction and it is possible that none of our product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval or clearance. We have only limited experience in filing and supporting the applications necessary to gain regulatory approvals and expect to rely on third-party CROs or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the biologic manufacturing process to and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining regulatory approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. 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 BLA, or equivalent application types, may cause delays in the approval or rejection of an application. FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. Our product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a BLA or other submission or to obtain regulatory approval in the United States or elsewhere;
- FDA or comparable foreign regulatory authorities may fail to approve our manufacturing processes or facilities; and
- the approval policies or regulations of FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, may impose certain post-marketing requirements that impose limits on our marketing and distribution activities, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenue will be materially impaired.

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 any potential marketing approval.

As with many pharmaceutical and biological products, treatment with our product candidates may produce undesirable side effects or adverse reactions or events. Although preclinical safety and biodistribution testing conducted on AAV vectors and data from previous clinical trials of other AAV vectors suggest that our AAV capsids may be well tolerated, known adverse side effects that could result from treatment with AAV vectors include an immunologic reaction to the capsid protein or gene at early time points after administration. . For example, in our recently discontinued Phase 1/2 clinical trial of DTX101 in hemophilia B, we observed elevated laboratory 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. If our vectors demonstrate a similar effect, or other adverse events, we may be required to halt or delay further clinical development of our product candidates. In addition, theoretical adverse 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. If any such adverse events occur, our clinical trials could be suspended or terminated and FDA, the EMA or other foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The product-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Genetically defined diseases may have relatively low prevalence and it may be difficult to identify patients with the disease, which together with other factors have in the past and may in the future lead to delays in enrollment for our trials.

Genetically defined diseases generally, and especially those for which our current product candidates are targeted, may have relatively low prevalence. For example, we estimate that there are approximately 10,000 patients worldwide with OTC deficiency, 8,000 of whom we estimate have late-onset OTC deficiency, which is our target population, 6,000 patients worldwide with GSDIa, approximately 2,000 worldwide patients with citrullinemia type I, more than 50,000 patients worldwide with PKU, and more than 50,000 Wilson disease patients worldwide. In addition, approximately 25% of potential patients in the United States have neutralizing antibodies that will significantly affect our product candidates' therapeutic efficacy. As a result, we will be required to screen for, and exclude from our clinical trials, patients with neutralizing antibodies to the product candidate that is subject to the clinical trial with specific assays developed for each clinical trial. Moreover, following administration of any AAV vector, patients are likely to develop neutralizing antibodies specific to the vector administered. These could be significant obstacles to the timely recruitment and enrollment of a sufficient number of eligible patients into our trials. For example, we experienced slower than expected patient enrollment in our recently discontinued Phase 1/2 clinical trial of DTX101 and we may experience similar delays in any of our future clinical trials. Patient enrollment may be affected by other factors including:

- the severity of the disease under investigation;
- design of the study protocol;
- the eligibility criteria for the study;
- the perceived risks, benefits and convenience of administration of the product candidate being studied;
- our efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians; and
- the proximity and availability of clinical trial sites to prospective patients.

We intend to engage third parties to develop companion diagnostics for use in our clinical trials to screen for neutralizing antibodies, but such third parties may not be successful in developing or administering such companion diagnostics in a timely manner, or at all. The lack of a suitable companion diagnostics would create difficulty in identifying patients with pre-existing neutralizing antibodies to be excluded from our clinical trials. Our inability to enroll a sufficient number of patients with the applicable genetic alteration for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Further, if we are unable to include patients with the applicable genetic alteration, this could compromise our ability to seek participation in FDA's expedited review and approval programs, including Breakthrough Therapy Designation and Fast Track Designation, or otherwise to seek to accelerate clinical development and regulatory timelines.

If we are unable to identify, source, and develop effective predictive 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 currently anticipate that we will need companion diagnostics to determine whether or not we can dose a particular patient with each of our products. We expect to use predictive biomarkers to identify the right patients for certain of our product candidates. For example, to evaluate therapeutic response of DTX301, we plan to measure ammonia levels and other biomarkers, including ^{13}C-acetate, which are established measures of OTC deficiency disease status and ureagenesis. We cannot assure you that ^{13}C-acetate or any other future potential biomarker will in fact prove predictive, be reliably sourced, or be accepted 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 DTX301. 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 intend to enter into agreements with third parties for the automation, characterization and validation, of our companion diagnostic and the manufacture of its critical reagents. However, we may be unable to enter into any such agreement on favorable terms, or at all.

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.

Positive results from early preclinical studies of our product candidates are not necessarily predictive of the results of later preclinical studies and clinical trials of our product candidates. If we cannot replicate the positive results from our earlier preclinical studies of our product candidates in our later preclinical studies and clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.

Positive results from our preclinical studies of our product candidates, and any positive results we may obtain from our early clinical trials of our product candidates, may not necessarily be predictive of the results from required later preclinical studies and clinical trials. Similarly, even if we are able to complete our planned preclinical studies or clinical trials of our product candidates according to our current development timeline, the positive results from our preclinical studies and clinical trials of our product candidates may not be replicated in subsequent preclinical studies or clinical trial results. For instance, in our in our recently discontinued Phase 1/2 clinical trial of DTX101 in hemophilia B, we demonstrated positive results in our preclinical studies but were unable to achieve those results later in the clinical study.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, non-clinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or EMA approval.

A Breakthrough Therapy Designation by FDA for our product candidates may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek a Breakthrough Therapy Designation for some of our product candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by FDA may also be eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under non-expedited FDA review procedures and does not assure ultimate approval by FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, FDA may later decide that the drugs no longer meet the conditions for qualification.

A Fast Track Designation by FDA may not actually lead to a faster development or regulatory review or approval process.

We sought and received Fast Track Designation for DTX301 and we may seek Fast Track Designation for some of our other product candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for Fast Track Designation. FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that FDA would decide to grant it. Even though we have obtained Fast Track Designation for DTX301 and even if we receive Fast Track Designation for our other product candidates, we may not experience a faster development process, review or approval compared to non-expedited FDA review procedures. In addition, FDA may withdraw Fast Track Designation for DTX301 or any other product candidate that is granted if it believes that the designation is no longer supported by data from our clinical development program.

We have sought and received Orphan Drug Designation for DTX301 and DTX401 in the United States and Europe, and we may seek Orphan Drug Designation for some of our other product candidates and we may be unsuccessful or may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for market exclusivity.

As part of our business strategy, we have sought and received Orphan Drug Designation for DTX301 and DTX401 in the United States and Europe. We may seek Orphan Drug Designation for our other product candidates and we may be unsuccessful or unable to maintain the associated benefits. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs intended to treat relatively small patient populations as orphan drugs. Under the U.S. Orphan Drug Act, FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax credits for qualified clinical research costs, and prescription drug user-fee waivers.

Similarly, in the European Union, the European Commission grants Orphan Drug Designation after receiving the opinion of the EMA's Committee for Orphan Medicinal Products on an Orphan Drug Designation application. In the European Union, Orphan Drug Designation is intended to promote the development of drugs that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the European Union and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). Additionally, orphan designation is granted for drugs intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug. In the European Union, Orphan Drug Designation entitles a party to financial incentives such as reduction of fees or fee waivers.

Generally, if a drug with an Orphan Drug Designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the EMA or FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. If our competitors are able to obtain orphan drug exclusivity prior to use, for products that constitute the same drug and treat the same indications as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority

for a significant period of time. The applicable period is seven years in the United States and ten years in the European Union. The European Union exclusivity period can be reduced to six years if a drug no longer meets the criteria for Orphan Drug Designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

Even though we have obtained Orphan Drug Designations for DTX301 and DTX401, and even if we obtain orphan drug exclusivity for DTX301 and other product candidates, that exclusivity may not effectively protect DTX301, DTX401 or our other product candidates from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, FDA can subsequently approve a later application for the same drug for the same condition if FDA concludes that the later drug is clinically superior in that it is shown to be safer in a substantial portion of the target populations, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the United States may be lost if FDA later determines that the request for designation was materially defective or if we are unable to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. 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. While we intend to seek Orphan Drug Designation for our other product candidates in addition to DTX301 and DTX401, we may never receive such designations. Even if we do receive such designations, there is no guarantee that we will enjoy the benefits of those designations.

Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

If FDA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the biologic will be governed by, and subject to, extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current Good Manufacturing Practices, or cGMPs, and Good Clinical Practices, or GCPs, for any clinical trials that we conduct post-approval. 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 may include conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase IV clinical trials, and surveillance to monitor the safety and efficacy of the product. FDA also may place other conditions on approvals including the requirement for a risk evaluation and mitigation strategy, or REMS, to assure the safe use of the product. If FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS before it can obtain approval. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Later discovery of previously unknown problems with a product candidate, including adverse events of unanticipated severity or frequency, or with our manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the drug, withdrawal of the drug from the market, or voluntary drug recalls;
- fines, warning letters or holds on clinical trials;
- refusal by FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of drug approvals or biologics licenses;
- drug seizure or detention, or refusal to permit the import or export of drugs; or
- injunctions or the imposition of civil or criminal penalties.

FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Risks Related to Manufacturing and Commercialization

Gene therapy products are novel, complex, expensive and difficult to manufacture. We could experience manufacturing problems that result in delays in our development or commercialization programs or otherwise harm our business.

The manufacturing process used to produce our product candidates is complex, novel 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 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 ours generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product 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 our manufacturing processes, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements. We also may not be able to complete scaling up of our facility in Woburn, MA, and this facility may not enable the expansion of our internal manufacturing process discovery and development to the extent we anticipate, or at all.

Any problems in our manufacturing process or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs. Problems in our manufacturing process could restrict our ability to meet market demand for our products.

Delays in obtaining a biologics license or disruptions in our manufacturing process may delay or disrupt our commercialization efforts. To date, no cGMP gene therapy manufacturer in the United States has received approval from FDA for the manufacture and commercialization of a gene therapy product.

Before we can begin to commercially manufacture our product candidates in the facility of a contractor or collaborator, or if we ever establish our own facility, we must obtain a biologics license from FDA. The biologics license is a determination that the product, the manufacturing process, and the manufacturing facility meet applicable requirements to ensure continued safety, purity and potency of the product. It is possible that FDA will not accept a future registration package in support of a license application for any of one or more reasons, including the safety, purity, and potency of the product candidate, the degree of product characterization, elements of the design or execution of the previous trials or safety concerns, or other trial results. Even if we receive regulatory approval for any of our product candidates, we will need to evaluate the formulation, stability and reproducibility of the formulated drug or drug product for commercial manufacturing. An MAA must also be submitted and approved by the appropriate European Union regulatory authority, and the product candidate must be manufactured in accordance with the approved application. To date, no cGMP gene therapy manufacturer in the United States has received approval from FDA for the manufacture and commercialization of a gene therapy product and, therefore, the timeframe required for us to obtain such approval is uncertain.

We expect our manufacturing strategy will involve the use of one or more CMOs as well as establishing our own capabilities and infrastructure, including at our Woburn, MA facility where we will support continued innovation in vector optimization and development of manufacturing processes required for IND-enabling studies and the reliable production of high quality AAV vectors at commercial scale. 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

never be successful 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 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 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.

In addition, the manufacturing process for any products that we may develop is subject to FDA and foreign regulatory authority approval process, and we will need to contract with manufacturers who can meet all applicable FDA and foreign regulatory authority requirements on an ongoing basis. If we or our CMOs are unable to reliably produce products to specifications acceptable to FDA or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our CMOs will be able to manufacture the approved product to specifications acceptable to FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations and growth prospects.

We intend to produce and to rely on third parties to produce our product candidates and other key materials, but we and these third parties have minimal or no experience producing our product candidates or other materials for late-stage clinical use or at commercial scale, and may not achieve the necessary regulatory approvals or produce our products or other materials at the quality, quantities, locations and timing needed to support development or commercialization.

Manufacturing of our product candidates is complex and any manufacturer with whom we may enter into an agreement may not have the expertise necessary to or be able to manufacture our product candidates at a cost or in quantities or on timelines necessary for the successful commercialization of our product candidates. If we successfully commercialize any of our product candidates, we will be required to establish commercial manufacturing capabilities, which we expect will rely on one or more third parties, and there is no guarantee that any such third parties will be able to do this in a timely manner, or at all. In addition, in the event that our product development pipeline increases and matures, we will have a greater need for clinical trial and commercial manufacturing capacity. Given that no gene therapy product has been approved in the United States, and only one has been approved in the European Union, there are few manufacturers with expertise in the manufacture of gene therapy products at late-stage clinical or commercial scale.

Although we have made, and expect to continue to make, substantial investments to develop manufacturing processes designed to produce AAV vectors at commercial scale, we do not have experience in manufacturing gene therapy products at commercial scale. We also have no experience in manufacturing any other pharmaceutical or biological products on a commercial scale and our potential suppliers will have to construct and validate new commercial manufacturing facilities and obtain regulatory approvals for the facilities before being able to produce our product candidates and there can be no assurance that they will succeed in doing so. Although we have specifically invested in developing expertise in manufacturing processes and have hired a team with extensive experience in production of product candidates for clinical use because we believe that these processes will be vital to support manufacture at late-stage clinical scale or, if approved, at commercial scale, we cannot assure you that our experience and expertise at manufacturing our product candidates on a small, clinical scale will be in fact sufficient to manufacture our products at late-stage clinical scale or, if approved, commercial scale. If our third-party manufacturers are unable to produce our viral vectors or product candidates in the necessary quantities, or in compliance with cGMP, or other pertinent regulatory requirements, such as stability, expiry or potency requirements or specifications, and within our planned time frame and cost parameters, the development and sales of our products, if approved, may be materially harmed.

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. In addition, we have not completed the development, characterization and validation activities necessary for commercial and regulatory approvals. If any of our manufacturing partners does not obtain such regulatory approvals for their facilities, our commercialization efforts will be harmed. In addition, any significant disruption in our supplier relationships could harm our business. We source key materials from third parties, either directly through agreements with suppliers or indirectly through our manufacturers who have agreements with suppliers. There are a small number of suppliers for certain key materials that are used to manufacture our product candidates. Such suppliers may not sell these key materials to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these key materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these key materials.

Any contamination in our or our third parties' manufacturing process, shortages of raw materials or failure of any of our key suppliers to deliver necessary components of our platform could result in delays in our clinical development or marketing schedules.

Given the nature of biologics manufacturing, there is a risk of contamination. Any contamination could materially adversely affect our or our third-party vendor's ability to produce our gene therapies on schedule and could therefore harm our results of operations and cause reputational damage.

Some of the raw materials required in our and our third-party vendors manufacturing processes are derived from biological sources. We cannot assure you that we or our third-party vendors have, or will be able to obtain on commercially reasonable terms, or at all, sufficient rights to these materials derived from biological sources. Such raw materials are difficult to procure and may also be subject to contamination or recall. A material shortage, contamination, recall, or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt the clinical and commercial manufacturing of our product candidates, which could materially and adversely affect our operating results and development timelines.

We rely on third-party suppliers for the supply and manufacture of certain components of our technology. Specifically, we have only one source of supply for some of the materials used in the upstream and downstream steps of our manufacturing process. These suppliers are not required to give us advance notice in the event they discontinue supply of the relevant materials. Should our ability to procure these material components from our suppliers be compromised, our ability to continuously operate would be impaired until an alternative supplier is sourced, qualified and tested, which could limit our ability to produce a clinical and commercial supply of our product candidates and harm our business.

Our use of viruses, chemicals and other hazardous materials requires us to comply with regulatory requirements and exposes us to significant potential liabilities.

Our development and manufacturing processes involve the use of viruses, chemicals and other hazardous materials, and produce waste products. Accordingly, we are subject to federal, state and local laws and regulations in the United States, are subject to comparable regulations in Europe and are subject to other foreign regulations governing the use, manufacture, distribution, storage, handling, treatment and disposal of these materials. In addition to ensuring the safe handling of these materials, applicable requirements require increased safeguards and security measures for many of these agents, including controlling access and screening of entities and personnel who have access to them, and establishing a comprehensive national database of registered entities. In the event of an accident or failure to comply with environmental, occupational health and safety and export control laws and regulations, we could be held liable for damages that result, and any such liability could exceed our assets and resources.

Our estimates of the incidence and prevalence for target patient populations for some or all of our product candidates may be inaccurate. If the market opportunities for our product candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.

Our projections of both the number of people who have OTC deficiency, GSDIa, Wilson disease, hemophilia A, PKU, and citrullinemia type I, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. The precise incidence and prevalence for OTC deficiency and GSDIa are unknown. By our estimate, the number of addressable patients globally with late-onset OTC deficiency is approximately 8,000, with GSDIa is approximately 6,000, citrullinemia type I approximately 2,000, PKU more than 50,000, and more than 50,000 for Wilson disease. We estimate that the number of addressable patients with moderate to severe hemophilia A is approximately 10,300 in the United States, and approximately 35,800 globally.

The total addressable market opportunity for DTX301 for the treatment of patients with OTC deficiency, DTX401 for the treatment of GSDIa patients, DTX201 for the treatment of hemophilia A, DTX701 for the treatment of patients with Wilson disease, DTX501 for the treatment of patients with PKU, and DTX601 for the treatment of patients with citrullinemia type I will ultimately depend upon, among other things, the diagnosis criteria included in the final label for each of DTX301, DTX401, DTX201, DTX701, DTX501, and DTX601 if our product candidates are approved for sale for these indications, acceptance by the medical community and patient access, drug pricing and reimbursement. Additionally, approximately 25% of potential patients estimated to exist in the United States have neutralizing antibodies that will significantly affect our product candidates' therapeutic efficacy. Thus, the number of patients globally may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

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

Ethical, social and legal concerns about gene therapy could result in additional regulations restricting or prohibiting our products. Even with the requisite approvals from FDA in the United States, the EMA in the European Union and other regulatory authorities internationally, the commercial success of our product candidates will depend, in part, on the acceptance of physicians, patients and health care payors of gene therapy products in general, and our product candidates in particular, as medically necessary, cost-effective and safe. Any product that we commercialize may not gain acceptance by physicians, patients, health care payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of gene therapy products and, in particular, our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy, durability and safety of such product candidates as demonstrated in clinical trials;
- the potential and perceived advantages of product candidates over alternative treatments;
- the cost of treatment relative to alternative treatments;
- the clinical indications for which the product candidate is approved by FDA or the European Commission;
- patient awareness of, and willingness to seek, genotyping;
- the willingness of physicians to prescribe new therapies;
- the willingness of the target patient population to try new therapies;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of FDA, the EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- relative convenience and ease of administration;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party payor coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product will not be fully known until after it is launched.

Our gene therapy approach utilizes vectors derived from viruses, which may be perceived as unsafe or may result in unforeseen adverse events. Negative public opinion and increased regulatory scrutiny of gene therapy may damage public perception of the safety of our product candidates and adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.

Gene therapy remains a novel technology, with no gene therapy product approved to date in the United States and only one gene therapy product approved to date in the European Union. 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. In particular, our success will depend upon physicians who specialize in the treatment of genetic diseases targeted by our product candidates, prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments with which they are familiar and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, earlier gene therapy trials led to several well- publicized adverse events, including cases of leukemia and death seen in other trials using other vectors.

A public backlash developed against gene therapy following the death in September 1999 of a patient who had volunteered for a gene therapy clinical trial that utilized an adenovirus vector at University of Pennsylvania School of Medicine. Researchers at the university, led by James M. Wilson, M.D., Ph.D., the chair of our clinical advisory board, had infused the volunteer's liver with a gene aimed at reversing OTC deficiency. The procedure triggered an extreme immune-system reaction that caused multiple organ failure in a very short time, leading to the first death to occur as a direct result of a gene therapy experiment. In addition, in two gene therapy studies in 2003, 20 subjects treated for X-linked severe combined immunodeficiency using a murine gamma-retroviral vector showed correction of the disease. However, the studies were suspended by FDA after a child in France developed leukemia and ultimately four other subjects were found to have developed leukemia.

Although none of our current product candidates utilize the human adenovirus or murine gamma-retroviruses used in the above- mentioned 1999 or 2003 studies, our product candidates do use a viral vector delivery system. The risk of cancer 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 product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on 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 on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. For example, on June 27, 2017, we announced our plan to focus internal efforts on the advancement of three programs to key clinical milestones, DTX301 for OTC deficiency, DTX401 for GSDIa, and DTX201 for hemophilia A, but we may not have correctly determined the optimal allocation of resources. Our resource allocation decisions may cause us to fail to timely capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any products for which we obtain marketing approval.

For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the Affordable Care Act, was enacted to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. As implementation of the of the Affordable Care Act is ongoing, the law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, that while not a law, is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the Affordable Care Act. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In addition, Congress could consider subsequent legislation to replace elements of the Affordable Care Act that are repealed, or the President could sign additional Executive Orders affecting elements of the Affordable Care Act. The implications of a potential repeal and/or replacement of the Affordable Care Act, or of other actions by the President or Congress related to the Affordable Care Act, for our and our partners' business and financial condition, if any, are not yet clear.

Moreover, the Drug Supply Chain Security Act imposes new obligations on manufacturers of pharmaceutical products related to product tracking and tracing. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We are not sure whether additional legislative changes will be enacted, or whether the current regulations, guidance or interpretations will be changed, or what the impact of such changes on our business, if any, may be.

We face significant competition in an environment of rapid technological change and the possibility that our competitors may achieve regulatory approval before us or develop therapies that are more advanced or effective than ours, which may harm our business and financial condition, and our ability to successfully market or commercialize our product candidates.

The biotechnology and pharmaceutical industries, including the gene therapy field, are characterized by rapidly changing technologies, significant competition and a strong emphasis on intellectual property. We face substantial competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions, some or all of which may have greater access to capital or resources than we do.

We are aware of several companies focused on developing gene therapies in various indications using various modalities including AAV vectors, including Spark Therapeutics, Inc., Applied Genetic Technologies Corporation, Asklepios BioPharmaceutical, Inc., Audentes Therapeutics, Inc., Adverum Biotechnologies, Voyager Therapeutics, Inc., GenSight Biologies SA, NightstaRx Limited, Selecta Biosciences, Inc., REGENX, Vivet Therapeutics, bluebird bio, Inc. and uniQure as well as several companies addressing other methods for modifying genes and regulating gene expression. Any advances in gene therapy technology made by a competitor may be used to develop therapies that could compete against any of our product candidates. If any of our competitors obtain regulatory approval of a gene therapy product for a disease that our current or future product candidates target, it may significantly diminish the market opportunity for our competing product candidate. This risk is particularly applicable when the patient populations for a disease are very small, which is the case for our product candidates, and in the field of gene therapy where a single administration may be sufficient to durably treat the disease.

The main competitors for our specific programs are as follows:

- DTX301: Arcturus Therapeutics Inc., Castle Creek Pharma LLC, PhaseRx, Inc., Selecta Biosciences, Inc., Synlogic, Inc., and Translate Bio.
- DTX401: CRISPR Therapeutics, Viking Therapeutics Inc., and new medical food products and longer-acting corn starch formulations.
- DTX201: Alnylam Incorporated, BioMarin Pharmaceutical Inc., Bioverativ, Freeline Therapeutics Ltd., LogicBio Therapeutics, Inc., Novo Nordisk S/A, Pfizer, Inc., Roche Holding AG, Sangamo Biosciences, Inc., Shire plc, Spark Therapeutics, Inc., Telethon Institute for Gene Therapy in collaboration with Bioverativ, and uniQure.
- DTX701: GMP-Orphan SAS, EffRx Pharmaceuticals, Kadmon Inc., Krisani Bio, Inc., Vivet Therapeutics, and Wilson Therapeutics AB.
- DTX501: American Gene Technologies International, Inc., BioMarin, Inc., Codexis, Inc., Synlogic, Inc. and Synthetic Biologics, Inc.
- DTX601: PhaseRx, Inc., Synlogic, Inc., and Vivet Therapeutics

To become and remain profitable, we must develop and eventually commercialize product candidates with significant market potential, which will require us to be successful in a range of challenging activities. These activities can include completing preclinical studies and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products that are approved and satisfying any post marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment.

If we obtain approval to commercialize our product candidates outside of the United States, in particular in the European Union, a variety of risks associated with international operations could harm our business.

We expect that we will be subject to additional risks in commercializing our product candidates outside the United States, including:

- different regulatory requirements for approval of drugs and biologics in foreign countries;
- our customers' ability to obtain reimbursement for our product candidates in foreign markets;
- reduced protection for intellectual property rights;
- existence of potentially relevant third-party intellectual property;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- import or export licensing requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- longer accounts receivable collection times;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- business interruptions resulting from geopolitical actions, including war and terrorism or natural disasters including earthquakes, typhoons, floods and fires, or from economic or political instability; and
- greater difficulty with enforcing our contracts in jurisdictions outside of the United States.

In some countries, particularly the countries in Europe, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Further, in many foreign countries it is common for others to engage in business practices that are prohibited by U.S. laws and regulations applicable to us, including the Foreign Corrupt Practices Act. Although we expect to implement policies and procedures designed to comply with these laws and policies, there can be no assurance that our employees, contractors and agents will comply with these laws and policies. If we are unable to successfully manage the challenges of international expansion and operations, our business and operating results could be harmed.

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

Our target patient populations are small, and accordingly, the pricing, insurance coverage, and reimbursement status of our product candidates, if approved, must be sufficient 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. We expect that coverage and reimbursement by government and private payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or will be reimbursed by government authorities, private health coverage insurers and other third-party payors. Coverage and reimbursement by a third-party payor may depend upon several factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

No uniform policy requirement for coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, obtaining coverage and reimbursement for a product from third-party payors is a time-consuming and costly process that could require us to provide to each different payor supporting scientific, clinical and cost-effectiveness data. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment. Assuming we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of our products. Therefore, coverage and adequate reimbursement is critical to new product acceptance. Additionally, there may be significant delays in obtaining coverage and reimbursement for newly approved biologics, and coverage may be more limited than the purposes for which the product is approved by FDA or comparable foreign regulatory authorities.

There is significant uncertainty related to third-party coverage and reimbursement of newly approved products. In the United States, third-party payors, including government payors such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered and reimbursed. The Medicare and Medicaid programs increasingly are used as models for how private payors and government payors develop their coverage and reimbursement policies. Currently, no gene therapy product has been approved for coverage and reimbursement by the Centers for Medicare & Medicaid Services, or CMS, the agency responsible for administering the Medicare program. It is difficult to predict what CMS will decide with respect to coverage and reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these types of products. Moreover, reimbursement agencies in the European Union may be more conservative than CMS. For example, several cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European Union Member States. It is difficult to predict what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Outside the United States, international operations generally are subject to extensive government price controls and other market regulations, and increasing emphasis on cost-containment initiatives in the European Union, Canada and other countries may put pricing pressure on us. For example, one gene therapy product was approved in the European Union in 2012 but is yet to be widely available commercially. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medical 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 product revenues.

Moreover, increasing efforts by government 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 approved and, as a result, they may not cover or provide adequate payment for our product candidates. Payors increasingly are considering new metrics as the basis for reimbursement rates, such as average sales price, average manufacturer price, or AMP, and actual acquisition cost. The existing data for reimbursement based on some of these metrics is relatively limited, although certain states have begun to survey acquisition cost data for the purpose of setting Medicaid reimbursement rates, and CMS has begun making pharmacy National

Average Drug Acquisition Cost and National Average Retail Price data publicly available on at least a monthly basis. Therefore, it may be difficult to project the impact of these evolving reimbursement metrics on the willingness of payors to cover candidate products that we or our partners are able to commercialize. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products such as ours.

If in the future we are unable to establish U.S. or global sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if and when they are approved and we may not be able to generate any revenue.

We do not currently have a sales or marketing infrastructure and have limited experience in the sale, marketing or distribution of drugs or biologics. To achieve commercial success for any approved product candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future drugs;
- the lack of complementary drugs to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability to us from these revenue streams is likely to be lower than if we were to market and sell any product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates. Further, our business, results of operations, financial condition and prospects will be materially adversely affected.

Risks Related to Our Financial Position and Need for Additional Capital

****Our management has concluded that a substantial doubt is deemed to exist concerning our ability to continue as a going concern.***

As of June 30, 2017, we reviewed the provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification Topic 205-40, Presentation of Financial Statements - Going Concern, or ASC 205-40, which requires management to assess our ability to continue as a going concern for one year after the date the financial statements are issued. As further discussed in "Note 1-Nature of the Business and Basis of Presentation" to our Condensed Consolidated Financial Statements in this Quarterly Report on Form 10-Q, substantial doubt is deemed to exist about the company's ability to continue as a going concern through August 8, 2018. Our financial statements do not include any adjustment relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might be necessary should we be unable to continue as a going concern. Our ability to continue as a going concern will require us to seek additional funding through public or private financings, debt financing, collaboration agreements or government grants. The reaction of investors to the inclusion of a going concern statement in this Quarterly Report on Form 10-Q, our current lack of cash resources and our potential inability to continue as a going concern may materially adversely affect our share price and our ability to raise additional funding, enter into strategic alliances and/or make our

scheduled debt payments on a timely basis or at all. No assurance can be given that additional funding will be available when required or on terms acceptable to us. The inability to obtain funding, as and when needed, would have a negative impact on our financial condition and ability to pursue our business strategies. If we become unable to continue as a going concern, we may have to liquidate our assets and investors may lose their investments. Additionally, the values we receive for our assets in liquidation or dissolution could be significantly lower than the values reflected in our financial statements.

We are a biopharmaceutical company with a limited operating history and have not generated any revenue from product sales. We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future and may not continue as a going concern.

We are a biopharmaceutical company with a limited operating history on which to base an investment decision. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We commenced operations in November 2013. Our operations to date have been limited primarily to organizing and staffing our company, business planning, raising capital, acquiring and developing product and technology rights and conducting research and development activities for our product candidates. We have never generated any revenue from product sales. We have not obtained regulatory approvals for any of our product candidates. We have funded our operations to date through proceeds from sales of preferred stock, from our IPO and from payments received in connection with our collaboration agreement with Bayer and, to a lesser extent, through borrowings under a loan and security agreement, as amended, that we entered into with Silicon Valley Bank, or SVB, in August 2014, as amended. We have incurred net losses in each year since our inception. As of June 30, 2017, we had an accumulated deficit of $126.0 million. Our net loss was $25.8 million and $21.6 million for the six months ended June 30, 2017 and 2016, respectively. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future and may not continue as a going concern. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect our research and development expenses to significantly increase in connection with beginning clinical trials of our product candidates. In addition, if we obtain marketing approval for our product candidates, we will incur significant sales, marketing and manufacturing expenses. As a public company, we will continue to incur costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical drugs, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any product revenue from our lead programs and product candidates, DTX301, DTX401, DTX201, DTX701, DTX501, and DTX601, and we do not know and do not expect to generate any revenue from the sale of our product candidates in the near future. We do not expect to generate significant product revenue unless and until we or our partners obtain marketing approval of and begin to sell DTX301, DTX401, DTX201, DTX701, DTX501, or DTX601, or one of our other product candidates. Our ability to generate product revenue depends on a number of factors, including, but not limited to, our ability to:

- initiate and successfully complete clinical trials that meet their clinical endpoints;
- initiate and successfully complete all safety studies required to obtain U.S. and foreign marketing approval for our product candidates;
- commercialize our product candidates, if approved, by developing a sales force or entering into additional collaborations with third parties; and
- achieve market acceptance of our product candidates in the medical community and with third-party payors.

We have entered into a collaboration agreement with Bayer for the development of DTX201 for hemophilia A. Absent our entering into a collaboration or partnership agreement for our remaining product candidates, we expect to incur significant sales and marketing costs as we prepare to commercialize our product candidates. Despite expending these costs, even if we initiate and successfully complete pivotal clinical trials of our product candidates and our product candidates are approved for commercial sale, our product candidates may not be commercially successful. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate product revenue, we will not become profitable and may be unable to continue operations without continued funding.

We will need additional funding in order to complete development of our product candidates and commercialize our products, if approved. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate some of our product development programs or commercialization efforts.

The development of pharmaceutical drugs is capital-intensive. We initiated a Phase 1/2 open-label clinical trial of DTX301 for OTC deficiency in December 2016. We are in IND-enabling activities to support IND filings for DTX401 for GSDIa and DTX201 for hemophilia A by early 2018, and are in candidate selection activities for DTX701, and expect to select a development candidate for DTX701 by the first half of 2018. We will also continue our ongoing follow-up of the six patients dosed in our recently discontinued Phase 1/2 clinical trial of DTX101 in hemophilia B and our ongoing extension study which will monitor all patients dosed for up to five years post dosing. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate clinical trials of and seek marketing approval for our product candidates. In addition, depending on the status of regulatory approval or, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of Bayer, or other collaborators. We may also need to raise additional funds sooner if we choose to pursue additional indications or geographies for our product candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate certain of our research and development programs or future commercialization efforts.

We expect that our existing cash, cash equivalents and marketable securities totaling $47.5 million and payments expected to be received in connection with our collaboration agreement with Bayer, including reimbursements and $15 million in milestones, will enable us to fund our operating expenses and capital expenditure requirements to the end of 2018. Without the milestones, the company would be able to fund operations to mid-2018. This raises substantial doubt of our ability to operate as a going concern for a period of one year from the issuance of these financial statements. See Note 1 to the condensed consolidated financial statements for management's plans. Our future capital requirements will depend on and could increase significantly as a result of many factors, including:

- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the scope, prioritization and number of our research and development programs;
- the success of our collaboration with Bayer;
- the success of our development, and the subsequent timing and outcome of regulatory clearance or approval, of companion diagnostics for use as screening criteria for potential patients;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration agreements we obtain;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of establishing or contracting for manufacturing capabilities if we obtain regulatory clearances to manufacture our product candidates;
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory clearances to market our product candidates; and
- our ability to establish and maintain healthcare coverage and adequate reimbursement.

Identifying potential product candidates and conducting preclinical development testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenue, if any, will be derived from product sales that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to complete development of our product candidates and commercialize our products, if approved.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. Dislocations in the financial markets have generally made equity and debt financing more difficult to obtain and may have a material adverse effect on our ability to meet our fundraising needs. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, 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. The incurrence of indebtedness would 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 could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or 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.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate 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.

Without additional funding, we may not have sufficient cash on hand or be able to generate sufficient cash flow from operations to meet our cash requirements over the next twelve months. These uncertainties raise substantial doubt about our ability to continue as a going concern. Our consolidated financial statements do not include any adjustments that might be necessary if we are unable to continue as a going concern.

The terms of our loan and security agreement may restrict our ability to engage in certain transactions.

In August 2014, we entered into a loan and security agreement with SVB. Pursuant to the terms of the loan and security agreement, as amended, subject to certain exceptions, we cannot engage in certain transactions unless certain conditions are met or we receive the prior approval of SVB. Such transactions include:

- disposing of our business or certain assets;
- changing our business, management, ownership or business locations;
- incurring additional debt or liens or making payments on other debt;
- making certain investments and declaring dividends;
- acquiring or merging with another entity;
- engaging in transactions with affiliates; or
- encumbering intellectual property.

If SVB does not provide its consent to such actions, we could be prohibited from engaging in transactions that could be beneficial to our business and our stockholders unless we were to repay the loans, which may not be desirable or possible. The loan and security agreement is collateralized by a pledge of substantially all of our assets, except for intellectual property. If we were to default under the loan and security agreement, including for an inability to repay amounts as they become due or if there is a material adverse change in our business, operations, or condition (financial or otherwise), and we were unable to obtain a waiver for such a default, SVB would have a right to accelerate our obligation to repay the entire loan and foreclose on these assets in order to satisfy our obligations under the loan and security agreement. In addition, SVB would also have the right to place a hold on our accounts maintained at SVB and refuse to fund any then unfunded commitments under the loan and security agreement. Any such action on the part of SVB against us could have a materially adverse impact on our business, financial condition and results of operations.

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

Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, contain rules that limit the ability of a company that undergoes an "ownership change" to utilize its net operating loss and tax credit carry forwards and certain built-in losses recognized in years after the ownership change. An "ownership change" is generally defined as any change in ownership of more than 50% of a corporation's stock over a rolling three-year period by stockholders that own (directly or indirectly) 5% or more of the stock of a corporation, or arising from a new issuance of stock by a corporation. If an ownership change occurs, Section 382 generally imposes an annual limitation on the use of pre-ownership change net operating losses, credits and certain other tax attributes to offset taxable income earned after the ownership change. The annual limitation is equal to the product of the applicable long-term tax exempt rate and the value of the Company's stock immediately before the ownership change. This annual limitation may be adjusted to reflect any unused annual limitation for prior years and certain recognized built-in gains and losses for the year. In addition, Section 383 generally limits the amount of tax liability in any post-ownership change year that can be reduced by pre-ownership change tax credit carryforwards. This could result in increased U.S. federal income tax liability for us if we generate taxable income in a future period. Limitations on the use of NOLs and other tax attributes could also increase our state tax liability. The use of our tax attributes will also be limited to the extent that we do not generate positive taxable income in future tax periods. As a result of these limitations, we may be unable to offset future taxable income (if any) with losses, or our tax liability with credits, before such losses and credits expire.

As of December 31, 2016, we had federal and state net operating loss carryforwards of $73.1 million and $73.5 million, respectively, both of which begin to expire in 2033. Our ability to utilize those net operating loss carryforwards could be limited by an "ownership change" as described above, which may increase our federal income tax liability. The completion of our recent IPO, together with private placements and other transactions that have occurred since our inception, may have triggered such an ownership change pursuant to Section 382. Any such limitation, whether as the result of our IPO, prior private placements, sales of our common stock by our existing stockholders or additional sales of our common stock by us, could have a material adverse effect on our results of operations in future years. We have not completed a study to assess whether an ownership change for purposes of Section 382 has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such study.

Risks Related to Our Relationships with Third Parties

Our executive officers, directors, principal stockholders and their affiliates exercise significant influence over our company, which could delay or prevent a change in corporate control.

As of August 1, 2017, the existing holdings of our executive officers, directors, principal stockholders and their affiliates, including entities affiliated with FMR LLC, or FMR, investment funds affiliated with OrbiMed Advisors LLC, or OrbiMed, and New Leaf Venture Partners, LLC will represent beneficial ownership, in the aggregate, of approximately 57% of our outstanding common stock. As a result, these stockholders, if they act together, will be able to influence our management and affairs and the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. This concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. We may enter into collaborations and partnerships for our programs and pipeline intended to allow us to leverage the resources and expertise of strategic collaborators or partners.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate

to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

In addition, our collaboration with Bayer and any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

We expect to rely on third parties to conduct our preclinical studies and clinical trials for our product candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We do not have the ability to independently conduct preclinical and clinical trials. We expect to rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct preclinical studies and clinical trials for our product candidates. We expect to rely heavily on these parties for execution of preclinical and clinical trials for our product candidates and control only certain aspects of their activities. Nevertheless, we will be responsible for ensuring that each of our preclinical and clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards and our reliance on CROs will not relieve us of our regulatory responsibilities. For any violations of laws and regulations during the conduct of our preclinical and clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution.

We and our CROs will be required to comply with regulations, including GCPs, for conducting, monitoring, recording and reporting the results of preclinical and clinical trials to ensure that the data and results are scientifically credible and accurate and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any drugs in clinical development. FDA enforces GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, FDA will determine that any of our future clinical trials will comply with GCPs. In addition, our clinical trials must be conducted with product candidates produced in accordance with the requirements in cGMP regulations. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action. We also are required to register our ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Although we intend to design the clinical trials for our product candidates, CROs will conduct all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future preclinical and clinical trials will also result in less direct control over the management of data developed through preclinical and clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical and clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs do not perform preclinical and clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our product candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our product candidates, or our development programs may be materially and irreversibly harmed. If we are unable to rely on preclinical and clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct and this could significantly delay commercialization and require significantly greater expenditures.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs 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 clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any preclinical studies or clinical trials with which such CROs are associated with may be extended, delayed or terminated. In such cases, we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, we believe that our financial results and the commercial prospects for our product candidates in the subject indication could be harmed, our costs could increase and our ability to generate revenue could be delayed.

We depend on third parties, including researchers and sublicensees, who are not under our control.

Since we are party to a collaboration agreement for the development of DTX201 with Bayer and rely on University of Pennsylvania School of Medicine to conduct preclinical studies for certain of our product candidates, we depend upon our sublicensee and independent investigators and scientific collaborators and other universities and medical institutions or private physician scientists, to advise us and to conduct our preclinical studies and clinical trials under agreements with us, including by developing and running screening assays for prospective patients in our clinical studies. University of Pennsylvania School of Medicine currently conducts some of our clinical assays pursuant to a sponsored research agreement. These collaborators are not our employees and we cannot control the amount or timing of resources that they devote to our programs or the timing of their procurement of clinical-trial data or their compliance with applicable regulatory guidelines. Should any of these scientific advisors or those of our sublicensee become disabled or die unexpectedly, or should they fail to comply with applicable regulatory guidelines, we or our sublicensee may be forced to scale back or terminate development of that program. They may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking those programs ourselves. These collaborators may also have relationships with other commercial entities, some of which may compete with us. Failing to devote sufficient time and resources to our program or product candidates, or substandard performance and failure to comply with regulatory guidelines, could result in delay of any FDA applications and our commercialization of the product candidate involved. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. In addition, we will be unable to prevent them from establishing competing businesses or developing competing products. For example, if a key scientist acting as a principal investigator in any of our clinical trials identifies a potential product or compound that is more scientifically interesting to his or her professional interests, his or her availability to remain involved in our clinical trials could be restricted or eliminated. If any of the foregoing were to become inaccessible or terminated, it would be difficult for us to develop and commercialize our biologic product candidates.

We rely on third parties to conduct some aspects of our vector production, product manufacturing, reagent manufacturing, protocol development, research, and preclinical and clinical testing, and these third parties may not perform satisfactorily.

We do not currently independently conduct all aspects of our vector production, product manufacturing, reagent manufacturing, protocol development, research and monitoring and management of our ongoing preclinical studies and clinical trials. We currently rely, and expect to continue to rely, on third parties with respect to these items, and control only certain aspects of their activities.

Most of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, our product candidate activities may be delayed. Our reliance on these third parties for research and development activities, including the conduct of any IND-enabling studies, reduces our control over these activities but does not relieve us of our responsibility to ensure compliance with all required legal, regulatory and scientific standards and any applicable trial protocols. For example, for product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our IND-enabling studies and clinical trials are conducted in accordance with the trial plan and protocols.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, or if there are process deviations that result in noncompliance with stability requirements or specifications, we may be delayed in completing, or unable to complete, the preclinical studies and clinical trials required to support future IND submissions and approval of our product candidates.

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical trials. There are a small number of suppliers for certain capital equipment and raw materials that we use to manufacture our product candidates. Such suppliers may not sell these raw materials to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Any significant delay in the supply of a product candidate, or the raw material components thereof for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates. If our manufacturers or we are unable to purchase these raw materials after regulatory approval has been obtained for our product candidates, our ability to commercially launch and/or generate revenues from the sale of any of our approved products would be impaired. Reliance on third-party manufacturers entails exposure to risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- we may be unable to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- reduced control over the manufacturing process for our product candidates as a result of using third-party manufacturers for all aspects of manufacturing activities;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that may be costly or damaging to us or result in delays in the development or commercialization of our product candidates; and
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including regulatory inspections or the bankruptcy of the manufacturer or supplier.

Any of these events could lead to delays in the development of our product candidates, including delays in our clinical trials, or failure to obtain regulatory approval for our product candidates, or it could impact our ability to successfully commercialize our current product candidates or any future products. Some of these events could be the basis for FDA or other regulatory action, including injunction, recall, seizure or total or partial suspension of production.

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Although we do not currently have any drugs on the market, once we begin commercializing our product candidates, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our product candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations in the U.S., include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false of fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal physician payment transparency requirements, sometimes referred to as the "Sunshine Act" under the Affordable Care Act, require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report to the Department of Health and Human Services information related to physician payments and other transfers of value and the ownership and investment interests of such physicians and their immediate family members; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales team, were to be found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

We may in the future form strategic alliances or acquire businesses or products or product candidates and we may not realize the benefits of such acquisitions or arrangements.

We may acquire additional businesses or products or product candidates, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them

with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new drugs resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

Risks Related to Intellectual Property

If we are unable to adequately protect our proprietary technology or obtain and maintain patent protection for our technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar to ours and our ability to successfully commercialize our technology and product candidates may be impaired.

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection in the United States and other countries for our current product candidates and future products, as well as our core technologies, including our manufacturing know-how. We expect to protect our proprietary and intellectual property position by, among other methods, filing patent applications in the United States and abroad related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

We have in-licensed patents and patent applications owned by the Trustees of the University of Pennsylvania, or the University of Pennsylvania, relating to various AAV vectors. These patents and patent applications are licensed or sublicensed to REGENX and sublicensed to us. Our sublicenses are exclusive, but limited to particular fields, such as *in vivo* gene therapy for OTC deficiency, GSDIa, hemophilia A, Wilson disease, PKU, citrullinemia type I, hemophilia B, and other future elected indications and are subject to certain retained rights. As described in "Business — Intellectual Property," most of these patents will expire in 2022, although some will expire later. In particular, any patent issuing on our licensed patent application relating to nucleic acid sequences encoding human ornithine transcarbamylase, should any patent issue, would not be expected to expire before 2035. The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation.

The degree of patent protection we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our licensed patents have, or that any of our pending licensed patent applications that mature into issued patents will include, claims with a scope sufficient to protect our current and future product candidates or otherwise provide any competitive advantage. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally twenty years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Moreover, our exclusive license is subject to retained rights, which may adversely impact our competitive position. As a result, our licensed patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing products similar to our product candidates, including biosimilar versions of such products. In addition, the patent portfolio licensed to us is, or may be, licensed to third parties, such as outside our field, and such third parties may have certain enforcement rights. Thus, patents licensed to us could be put at risk of being invalidated or interpreted narrowly in litigation filed by or against another licensee or in administrative proceedings brought by or against another licensee in response to such litigation or for other reasons.

Other parties have developed technologies that may be related or competitive to our own and such parties may have filed or may file patent applications, or may have received or may receive patents, claiming inventions that may overlap or conflict with those claimed in our own patent applications or issued patents. Publications of discoveries in the scientific literature often lag behind the actual discoveries and patent applications in the United States and in other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether the inventors of our licensed patents and applications were the first to make the inventions claimed in those patents or pending patent applications, or that they were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, and commercial value of our patent rights cannot be predicted with any certainty.

In addition, the patent prosecution 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. We cannot provide any assurances that we will be able to pursue or obtain additional patent protection based on our research and development efforts, or that any such patents or other intellectual property we generate will provide any competitive advantage. Patent prosecution is a lengthy

process and the scope of the claims initially submitted for examination may be significantly narrowed by the time they issue, if at all. Moreover, we do not have the right to control the preparation, filing and prosecution of patent applications, or to control the maintenance of the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be filed, prosecuted or maintained in a manner consistent with the best interests of our business. In addition, under our agreements with REGENX and the University of Pennsylvania, 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, REGENX and the University of Pennsylvania may have interests which differ from ours in determining whether and the manner in which to enforce such patents.

Even if we acquire patent protection that we expect should enable us to maintain competitive advantage, third parties, including competitors, may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. In litigation, a competitor could claim that our patents, if issued, are not valid for a number of reasons. If a court agrees, we would lose our rights to those challenged patents.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability and our licensed patents may be challenged in courts or patent offices in the United States and abroad. For example, we may be subject to a third-party submission of prior art to the U.S. Patent and Trademark Office, or USPTO, challenging the validity of one or more claims of our licensed patents. Such submissions may also be made prior to a patent's issuance, precluding the granting of a patent based on one of our pending licensed patent applications. We may become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging the patent rights of others from whom we have obtained licenses to such rights. Competitors may claim that they invented the inventions claimed in such issued patents or patent applications prior to the inventors of our licensed patents, or may have filed patent applications before the University of Pennsylvania did. A competitor may also claim that we are infringing its patents and that we therefore cannot practice our technology as claimed under our licensed patents, if issued. Competitors may also contest our licensed patents, if issued, by showing that the invention was not patent-eligible, was not novel, was obvious or that the patent claims failed any other requirement for patentability.

In addition, the University of Pennsylvania may in the future be subject to claims by former employees, collaborators or consultants asserting an ownership right in our licensed patents or patent applications, as a result of the work they performed on the University of Pennsylvania's behalf. An adverse determination in any such submission or proceeding may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar technology and therapeutics, without payment to us, or could limit the duration of the patent protection covering our technology and product candidates. Such challenges may also result in our inability to manufacture or commercialize our product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if they are unchallenged, our licensed patents and pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our licensed patents by developing similar or alternative technologies or therapeutics in a non-infringing manner. For example, a third party may develop a competitive therapeutic that provides benefits similar to one or more of our product candidates but that uses a vector or an expression construct that falls outside the scope of our patent protection or license rights. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our product candidates could be negatively affected, which would harm our business. Although currently all of our patents and patent applications are in-licensed, similar risks would apply to any patents or patent applications that we may own or in-license in the future.

We are required to pay certain royalties under our license agreements with third-party licensors, and we must meet certain milestones to maintain our license rights.

Under our license agreements with REGENX and the University of Pennsylvania, we will be required to pay royalties based on our revenues from sales of our products utilizing the technologies and products sublicensed by REGENX from the University of Pennsylvania and licensed directly to us by the University of Pennsylvania and these royalty payments could adversely affect the overall profitability for us of any products that we may seek to commercialize. These agreements contain diligence obligations and we may not be successful in meeting all of the obligations in the future on a timely basis or at all. For example, in order to maintain our license rights under our license agreement with the University of Pennsylvania, we need to use commercially reasonable efforts in the development and commercialization of our licensed product candidates. In order to maintain our license rights under our license agreements with REGENX, we will need to meet certain specified milestones, subject to certain cure provisions, in the development of our product candidates and in the raising of funding and use commercially reasonable efforts to develop, commercialize, market, promote and sell licensed products. If we fail to use commercially reasonable efforts as required by the license agreements with

REGENX and REGENX subsequently terminates one or both of our license agreements with REGENX for breach, REGENX will have the right to use certain of our intellectual property and technology going forward. We will need to outsource and rely on third parties for many aspects of the clinical development, sales and marketing of our products covered under our license agreements. Delay or failure by us or these third parties could adversely affect the continuation of our license agreements with third-party licensors.

All of our current product candidates are licensed from or based upon licenses from the University of Pennsylvania. If any of these license or sublicense agreements are terminated or interpreted to narrow our rights, our ability to advance our current product candidates or develop new product candidates based on these technologies will be materially adversely affected.

We now depend, and will continue to depend, on our licenses of the University of Pennsylvania technology through REGENX, as well as directly from the University of Pennsylvania, and potentially on other licensing arrangements or strategic relationships with third parties for the research, development, manufacturing and commercialization of our current product candidates. If any of our licenses or relationships or any in-licenses on which our licenses are based are terminated or breached, we may:

- lose our rights to develop and market our current product candidates;
- lose patent or trade secret protection for our current product candidates;
- experience significant delays in the development or commercialization of our current product candidates;
- not be able to obtain any other licenses on acceptable terms, if at all; or
- incur liability for damages.

Additionally, even if not terminated or breached, our intellectual property licenses or sublicenses may be subject to disagreements over contract interpretation which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations.

If we experience any of the foregoing, it could have a materially adverse effect on our business and could force us to cease operations which could cause you to lose all of your investment.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and future products and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and frequent litigation regarding patents and other intellectual property rights. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates, future products and technology, including interference or *inter partes* review proceedings before the USPTO. Our competitors or other third parties may assert infringement claims against us, alleging that our therapeutics, manufacturing methods, formulations or administration methods are covered by their patents. For example, we do not know which processes we will use for commercial manufacture of our future products, or which technologies owned or controlled by third parties may prove important or essential to those processes. Given the vast number of patents in our field of technology, we cannot be certain or guarantee that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Many companies have filed, and continue to file, patent applications related to gene therapy and orphan diseases. Some of these patent applications have already been allowed or issued and others may issue in the future. Since this area is competitive and of strong interest to pharmaceutical and biotechnology companies, there will likely be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. Furthermore, because patent applications can take many years to issue, may be confidential for 18 months or more after filing and can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use, sale or importation of our product candidates or future products. If a patent holder believes the manufacture, use, sale or importation of one of our product candidates or future products infringes its patent, the patent holder may sue us even if we have licensed other patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our licensed patent portfolio may therefore have no deterrent effect.

It is also possible that we have failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Moreover, it is difficult for industry participants, including us, to identify all third-party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify

relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale, importation or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our future products or the manufacture or use of our future products. We are aware of, for example, four third-party patent families that include issued U.S. patents with claims that, if valid and enforceable, could be construed to cover some of our product candidates, if and when approved, or their methods of manufacture or use. We are aware of an additional three 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 our product candidates.

Third parties may assert infringement claims against us based on existing intellectual property rights and intellectual property rights that may be granted in the future. If we were to challenge the validity of an issued U.S. patent in court, such as an issued U.S. patent of potential relevance to some of our product candidates or future products or manufacture or methods of use, we would need to overcome a statutory presumption of validity that attaches to every U.S. patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. There is no assurance that a court would find in our favor on questions of infringement or validity.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. If we are found, or believe there is a risk we may be found, to infringe a third party's intellectual property rights, we could be required or may choose to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any such license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. Without such a license, we could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our future products or force us to cease some of our business operations, which could materially harm our business. If we lose a foreign patent lawsuit, alleging our infringement of a competitor's patents, we could be prevented from marketing our therapeutics in one or more foreign countries and/or be required to pay monetary damages for infringement or royalties in order to continue marketing. Claims that we have misappropriated the confidential information, trade secrets or other intellectual property of third parties could have a similar negative impact on our business. Any of these outcomes would have a materially adverse effect on our business.

Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our future products or processes. Patent litigation is costly and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our licensed patents, any patents we may own or license in the future and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims. A court may disagree with our allegations, however, and may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the third-party technology in question. Further, such third parties could counterclaim that we infringe their intellectual property or that a patent we have asserted against them is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace. In addition, third parties may initiate legal proceedings against us to assert such challenges to our intellectual property rights. The outcome of any such proceeding is generally unpredictable. 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. Patents may be unenforceable if someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. It is possible that prior art of which we and the patent examiner were unaware during prosecution exists, which could render our licensed patents invalid. Moreover, it is also possible that prior art may exist that we are aware of but do not believe is relevant to our licensed patents, but that could nevertheless be determined to render those patents invalid. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review and equivalent proceedings in foreign jurisdictions, such as opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable.

An adverse result in any litigation or administrative proceeding could put one or more of our licensed patents at risk of being invalidated or interpreted narrowly. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of our licensed patents covering one of our product candidates, we would lose at least part, and perhaps all, of the patent protection covering such product candidate. Competing therapeutics may also be sold in other countries in which our patent coverage might not exist or be as strong. Any of these outcomes would have a materially adverse effect on our business.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation in certain countries, including the United States, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing or misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees on issued patents often must be paid to the USPTO and foreign patent agencies over the lifetime of the patent. While an unintentional lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, we may not be able to stop a competitor from marketing drugs that are the same as or similar to our product candidates, which would have a material adverse effect on our business.

Some intellectual property which we have in-licensed may have been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.

Many of the intellectual property rights we have licensed are generated through the use of U.S. government funding and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if we, or the applicable licensor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that

reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

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

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, the patent laws of some foreign countries do not afford intellectual property protection to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our licensed patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our licensed or owned inventions in all countries outside the United States. Competitors may use our technologies in jurisdictions where we have not pursued and obtained patent protection to develop their own therapeutics and, further, may export otherwise infringing products to territories where we have patent protection or license rights, if our ability to enforce our patents to stop infringing activities is inadequate. These therapeutics may compete with our product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in the major markets for our future products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our future products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a "first to file" system. The first-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and 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 harm our business, results of operations and financial condition.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening 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," and invalidated Myriad Genetics's patents on the BRCA1 and BRCA2 genes. Certain claims of our licensed patents relate to isolated AAV 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.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position may be harmed.

In addition to the protection afforded by patents, we rely upon unpatented trade secret protection, unpatented know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our contractors, collaborators, scientific advisors, employees and consultants and invention assignment agreements with our consultants and employees. We may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements, however, despite the existence generally of confidentiality agreements and other contractual restrictions. Monitoring unauthorized uses and disclosures is difficult and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the contractors, collaborators, scientific advisors, employees and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation. As a result, we could lose our trade secrets. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing or unwilling to protect trade secrets.

Our trade secrets could otherwise become known or be independently discovered by our competitors. Competitors could purchase our product candidates and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If our trade secrets are not adequately protected or sufficient to provide an advantage over our competitors, our competitive position could be adversely affected, as could our business.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of, or are in breach of non-competition or non-solicitation agreements with third parties.

We could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other proprietary information or materials of former employers, competitors or other third parties. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know-how or trade secrets of others without authorization in their work for us, we may in the future be subject to claims that we caused an employee to breach the terms of his or her confidentiality, non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information or materials of a former employer, competitor or other third party. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our product candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers or others. An inability to incorporate such technologies or features could have a material adverse effect on our business and may prevent us from successfully commercializing our product candidates. In addition, we may lose valuable intellectual property rights or personnel as a result of such claims. Moreover, any such litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent contractors. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our product candidates, which would have an adverse effect on our business, results of operations and financial condition.

Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business

We have recently reduced the size of our organization, and we may encounter difficulties in managing this development and restructuring, which could disrupt our operations. In addition, we may not achieve anticipated benefits and savings from the reduction.

On June 27, 2017, we announced the completion of a strategic review and our plan to focus internal efforts on the advancement of three programs to key clinical milestones, DTX301 for OTC deficiency, DTX401 for GSDIa, and DTX201 for hemophilia A. In connection with our reprioritization, we expect a reduction in approximately 25% of our workforce by the end of 2017, including workforce reductions and attrition. The workforce reduction will result in the loss of longer-term employees, the loss of institutional knowledge and expertise and the reallocation and combination of certain roles and responsibilities across the organization, all of which could adversely affect our operations. Given the complexity of our business, we must continue to implement and improve our managerial, operational and financial systems, manage our facilities and continue to recruit and retain qualified personnel. This will be made more challenging given the workforce reduction described above. As a result, 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 activities. Further, the restructuring and possible additional cost containment measures may yield unintended consequences, such as attrition beyond our intended workforce reduction and reduced employee morale. In addition, we may not achieve anticipated benefits from the workforce reduction. Due to our limited resources, we may not be able to effectively manage our operations or recruit and retain qualified personnel, which may result in weaknesses in our infrastructure and operations, risks that we may not be able to comply with legal and regulatory requirements, and loss of employees and reduced productivity among remaining employees. For example, the workforce reduction may negatively impact our clinical and regulatory functions, which would have a negative impact on our ability to successfully develop, and ultimately, commercialize our product candidates. If our management is unable to effectively manage this transition and workforce reduction and additional cost containment measures, our expenses may be more than expected and we may not be able to implement our business strategy. As a result, our future financial performance and our ability to commercialize our product candidates successfully would be negatively affected.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical, commercial and business development expertise of Dr. Annalisa Jenkins, our President and Chief Executive Officer, Dr. Samuel C. Wadsworth, our Chief Scientific Officer, Mary T. Thistle, our Chief Operating Officer, and Eric Crombez, our Chief Medical Officer, as well as the other principal members of our management, scientific, clinical and commercial team. Although we have entered into employment letter agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We also implemented a workforce reduction in June 2017 in connection with our completion of a strategic review and our plan to focus internal efforts on the advancement of three programs to key clinical milestones, DTX301 for OTC deficiency, DTX401 for GSDIa, and DTX201 for hemophilia A. With any workforce reduction, there is a risk to retention of employees, including executive officers, as well as the potential for disruption to business operations, initiatives, plans and strategies. Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize drugs. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the workforce reduction and the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. We have begun the process of documenting, reviewing and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, which will require annual management assessment of the effectiveness of our internal control over financial reporting. We recruited finance and accounting personnel with certain skill sets that we require as a public company. If we are unable to continue to attract and retain high quality personnel with these skill sets, our ability to maintain proper and effective internal control over financial reporting may be compromised.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our stock price and make it more difficult for us to effectively market and sell our service to new and existing customers.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the global financial crisis, could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Exposure to UK political developments, including the outcome of the UK referendum on membership in the European Union, could have a material adverse effect on us.

On June 23, 2016, a referendum was held on the United Kingdom's membership in the European Union, the outcome of which was a vote in favor of leaving the European Union. The United Kingdom's vote to leave the European Union creates an uncertain political and economic environment in the United Kingdom and potentially across other European Union member states, which may last for a number of months or years.

Article 50 of the Treaty of the European Union, or Article 50, allows a member state to decide to withdraw from the European Union in accordance with its own constitutional requirements. The formal process for leaving the European Union will be triggered only when the United Kingdom delivers an Article 50 notice to the European Council, although informal negotiations around the terms of any exit may be held before such notice is given. Delivery of the Article 50 notice will start a two-year period for the United Kingdom to exit from the European Union, although this period can be extended with the unanimous agreement of the European Council. Without any such extension (and assuming that the terms of withdrawal have not already been agreed), the United Kingdom's membership in the European Union would end automatically on the expiration of that two-year period.

The result of the referendum means that the long-term nature of the United Kingdom's relationship with the European Union is unclear and that there is considerable uncertainty as to when any such relationship will be agreed and implemented. In the interim, there is a risk of instability for both the United Kingdom and the European Union, which could adversely affect our results, financial condition and prospects.

It is currently expected that the UK government will shortly commence negotiations in connection with any exit from the European Union and will make a decision regarding the timing for giving an Article 50 notice. There is also considerable uncertainty as to whether, following any Article 50 notice being given, the arrangements for the United Kingdom to leave the European Union will be agreed upon within the two-year period and, if not, whether an extension of that time period would be agreed upon. It is also possible that the European Union will pressure the United Kingdom to exit prior to the end of the two-year period. There is also a risk of the United Kingdom's exit from the European Union being effected without mutually acceptable terms being agreed and that any terms of such exit could adversely affect our operating results, financial condition and prospects.

The political and economic instability created by the United Kingdom's vote to leave the European Union has caused and may continue to cause significant volatility in global financial markets and the value of the Pound Sterling currency or other currencies, including the Euro. Depending on the terms reached regarding any exit from the European Union, it is possible that there may be adverse practical and/or operational implications on our business.

Consequently, no assurance can be given as to the impact of the referendum outcome and, in particular, no assurance can be given that our operating results, financial condition and prospects would not be adversely impacted by the result.

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

Natural disasters could severely disrupt our operations 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 our manufacturing facilities, 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 may prove 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, could have a material adverse effect on our business.

Our internal computer systems, or those of our third-party CROs, CMOs, or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product candidates' development programs.

Despite the implementation of security measures, our internal computer systems and those of our third-party CROs, CMOs, and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for our product candidates 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 or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed.

Our employees, principal investigators, CROs, CMOs, and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, principal investigators, CROs, CMOs, and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the United States and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have a code of conduct applicable to all of our employees. However, it is not always possible to identify and deter misconduct by employees and other third parties and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any product candidates that we may develop.

We will face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any product candidates that we may develop. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any product candidates that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage when we begin clinical trials and if we successfully commercialize any product candidate. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological or hazardous materials.

Risks Related to Our Common Stock

We will incur significant costs as a result of operating as a public company and our management is required to devote substantial time to new compliance initiatives.

As a public company, we incur significant legal, accounting and other expenses due to our compliance with regulations and disclosure obligations applicable to us, including the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the Securities and Exchange Commission, or SEC, and the NASDAQ Stock Market LLC, or NASDAQ. The SEC and other regulators have continued to adopt new rules and regulations and make additional changes to existing regulations that require our compliance. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly. We expect these expenses to increase once we are no longer an "emerging growth company."

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue

to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for our stockholders.

Our stock price has been and is likely to be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. From October 22, 2015 through August 1, 2017, our stock price has traded at prices as low as $1.05 per share and as high as $15.55 per share. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price they paid for their shares. The market price for our common stock may be influenced by many factors, including:

- the success of competitive drugs or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or drugs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If few analysts commence coverage of us, the trading price of our stock would likely decrease. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated by-laws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders and the ability of our board of directors to issue preferred stock without stockholder approval. 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. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirors to negotiate with our board of directors, they would apply even if an offer rejected by our board of directors were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year in which we have total annual gross revenue of $1 billion or more; (ii) December 31, 2020; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- being permitted to present only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We may choose to take advantage of some, but not all, of the available exemptions. In particular, we provided only two years of audited financial statements and did not include all of the executive compensation information that would have been required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be our stockholders' sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. Additionally, under the loan and security agreement with SVB, we are currently restricted from paying cash dividends and we expect these restrictions to continue in the future. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

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

Sales of Unregistered Securities

None.

Use of Proceeds from Registered Securities

On October 27, 2015, we completed the initial public offering of our common stock and issued and sold 5,500,000 shares of our common stock at a public offering price of $13.00 per share. On November 25, 2015, the underwriters of the Company's IPO exercised their over-allotment option to purchase an additional 104,775 shares of common stock at the initial public offering price of $13.00 per share.

The offer and sale of all of the shares in the offering was registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-206911), which was declared effective by the SEC on October 21, 2015. Following the sale of the shares in connection with the closing of our initial public offering, the offering terminated. The offering commenced on October 21, 2015 and did not terminate until the sale of all of the shares offered. Goldman, Sachs & Co. and Citi Global Markets Inc. acted as joint book-running managers of the offering, and Wells Fargo Securities LLC, Canaccord Genuity Inc. and Cantor Fitzgerald & Co. acted as co-managers of the offering.

We received aggregate gross proceeds from the offering, including in connection with the exercise by the underwriters of their over-allotment option, of $72.9 million, or aggregate net proceeds of $64.6 million after deducting underwriting discounts and commissions of $5.1 million and offering expenses of $3.2 million. No payments for such expenses were made directly or indirectly to (i) any of our officers or directors or their associates, (ii) any persons owning 10% or more of any class of our equity securities or (iii) any of our affiliates.

As of June 30, 2017, we have used approximately $17.1 million of the net offering proceeds, primarily to fund our Phase 1/2 open-label clinical trial of DTX301 in OTC deficiency, IND enabling activities for DTX401 in GSDIa and our recently discontinued Phase 1/2 clinical trial of DTX101 for hemophilia B. No payments for such expenses were made directly or indirectly to (i) any of our officers or directors or their associates, (ii) any persons owning 10% or more of any class of our equity securities or (iii) any of our affiliates. The remaining portion of the net proceeds is included as cash and cash equivalents and marketable securities. We expect to continue to use the remaining net proceeds for our Phase 1/2 open-label clinical trial of DTX301 in OTC deficiency, preclinical and clinical development for DTX401 in GSDIa, our ongoing DTX101 for hemophilia B extension study which will monitor all six patients dosed in our recently discontinued Phase 1/2 clinical trial, and the preclinical and clinical development of our other product candidates.

Item 3. Defaults Upon Senior Securities.

None.

Item 4. Mine Safety Disclosures.

Not Applicable.

Item 5. Other Information.

None.

Item 6. Exhibits.

The exhibits filed as part of this Quarterly Report on Form 10-Q are set forth on the Exhibit Index, which is incorporated herein by reference.

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.

Company Name

Date: August 8, 2017

By: /s/ Annalisa Jenkins
Annalisa Jenkins
President and Chief Executive Officer
(Principal Executive Officer)

Date: August 8, 2017

By: /s/ Mary Thistle
Mary Thistle
Chief Operating Officer
(Principal Financial Officer)

Exhibit Index

Exhibit Number	Description
10.1*	Second Lease Amendment to the Lease Between Rivertech Associates II, LLC and the Company, dated April 28, 2017.
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1**	Certification of Principal Executive Officer Pursuant and Principal Financial Officer to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.

** The certifications furnished in Exhibit 32.1 hereto are deemed to accompany this Quarterly Report on Form 10-Q and will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

Exhibit 10.1

RIVERSIDE TECHNOLOGY CENTER

SECOND LEASE AMENDMENT

TO THE LEASE BETWEEN

RIVERTECH ASSOCIATES II, LLC AND DIMENSION THERAPEUTICS, INC.

This Second Lease Amendment (the "Second Amendment") entered into this 28th day of April, 2017 by and between **Rivertech Associates II, LLC,** a Massachusetts limited liability company with a principal address c/o The Abbey Group, 177 Huntington Avenue 24th Floor Boston, MA 02115 (herein the "Lessor"), and **Dimension Therapeutics, Inc.,** with a business address at 840 Memorial Drive Cambridge, Massachusetts (herein the "Lessee"); with respect to a certain Lease dated March 11, 2014 (the "Original Lease") for certain office and laboratory space in the building at 840 Memorial Drive Cambridge, Massachusetts, as amended by a certain First Lease Amendment dated October 22, 2014 (the "First Amendment"); collectively referred to herein as the "Existing Lease").

WHEREAS, Lessor and Lessee are the current parties to the Existing Lease; and,

WHEREAS, the current term under the Existing Lease is set to expire on January 31, 2018 (the "Current Term Expiration Date"); and,

WHEREAS, under the Existing Lease the Lessee leases and occupies approximately 14,949 rentable square feet of space in the Building, consisting of approximately 8,110 rentable square feet of space on the fourth floor of the Building, and approximately 6,839 rentable square feet of space on the second floor of the Building, (the " Existing Premises"); and,

WHEREAS, Lessor and Lessee seek by this current agreement to extend the Term of the lease and tenancy for one (1) additional period of two (2) years from the Current Term Expiration Date;

THEREFORE, in consideration of One ($1.00) Dollar and the other good and valuable consideration recited herein, effective and irrevocable as of the date hereof the Lessor and Lessee hereby agree as follows:

1. Modification to Existing Lease / Extension of Current Term

Lessee hereby extends its tenancy as to the Existing Premises for a twenty four (24) month period (the "Extended Term") from the Current Term Expiration Date through January 31, 2020 (the "Modified Term Termination Date").

2. Terms and Conditions

Lessee shall continue to lease the Existing Premises up to the Modified Term Termination Date, on the same terms and conditions of the Existing Lease with exception only for those provisions as to which Lessor and Lessee have already performed their obligations as of the date hereof (for example, Lessor has heretofore delivered the Existing Premises and Lessee has accepted the same).

The Existing Premises is leased in the same "AS/IS" condition as it is as of the execution of this Second Amendment, and Lessee acknowledges Lessor is under no obligation to make any improvements or modifications thereto, in any manner whatsoever.

Lessor and Lessee each acknowledge that to the best of the respective knowledge of each, there are no material defaults by either party presently existing under the Existing Lease.

3. Condition of Existing Premises

The Existing Premises shall be leased for the Extended Term in its "AS/IS" condition, in all respects, without any representations or warranties by Lessor of any kind or nature, except as otherwise currently exist in the Lease.

4. Annual Base Rent / Additional Rent / Security Deposit

A. Annual Base Rent

Annual Base Rent for the balance of the current Term up to the Current Term Expiration Date shall be as set forth in the Existing Lease.

Annual Base Rent for the Extended Term, commencing as of February 1, 2018, shall be as follows:

Extended Term Lease Year	Annual Base Rent	Monthly Installment
February 1, 2018 – January 31, 2019	$ 956,736.00	$ 79,728.00
February 1, 2019 – January 31, 2020	$ 986,634.00	$ 82,219.50

B. Additional Rent

In addition to Annual Base Rent, Lessee shall continue to be responsible to pay all Additional Rent, inclusive of "Additional Rent (Operating Expenses)" under Section 3 of the Existing Lease, and all "Additional Rent (Taxes)" under Section 4 thereof, as invoiced by Lessor up through the Extended Term Termination Date.

As the concept is used in the Lease to compute Additional Rent Lessee's allocable pro rata share ("Allocable Percentage") shall be as last stated under the First Amendment (i.e. a combined 11.54%).

C. Rent Payment and other Costs and Expenses

Determination and payment of all Annual Base Rent, Additional Rent and other sums due as Rent shall be payable and in all other respects shall be governed during the remainder of the current Term, and for the Extended Term, as contemplated under the Existing Lease, except to the extent modified and supplemented herein.

D. Security Deposit

The Security Deposit currently held by the Lessor shall continue to be held by Lessor as a Security Deposit during the Extended Term.

5. Permitted Uses

The Permitted Uses in the Basic Data of the Original Lease, and all conditions attached thereto, are hereby restated and affirmed and shall continue to govern the use and occupancy of the Existing Premises through to the end of the Extended Term (as it may be further extended hereunder).

6. Parking

Lessee shall have the right to continue to access twenty two (22) parking spaces (i.e. its currently permitted allocation) during the Extended Term (as it may be further extended hereunder), on the terms and conditions set forth in the First Amendment.

7. Brokers

The parties hereby agree there are no brokerage or other third-party fees or costs involved in this transaction other than to Transwestern RBJ, and each agrees to indemnify, defend and hold harmless the other from and against any other claims for brokerage fees, commissions or other such payments arising from this transaction. Commissions/fees owing to Transwestern RBJ from this transaction shall be paid by Lessor pursuant to a separate agreement between Lessor and said company.

8. Lessee's Further Option to Extend

Lessee, provided there is not then any existing default by Lessee under the Lease (beyond applicable notice grace and cure periods), and further provided there have not been any prior material defaults (beyond applicable notice, grace and cure periods) more than twice in any twelve (12) month period, shall have the option to further extend the Term of the Lease as to the Existing Premises (inclusive of any ROFO Space as may have been elected by Lessee under the provisions of the First Amendment). If timely elected the extension shall be for one (1) additional period of sixty (60) months (herein, the "Additional Term Extension Period") beginning as of the end of the Extended Term, at the then-current "Market Rent", including annual escalations thereon for each year of the Additional Term Extension Period (based on increases in the Consumer Price Index or fixed increases as the case may be as determined by then-prevailing market forces; but no less than an amount equal to the Annual Base Rent per square foot as of the final full

month of the last Lease Year of the Extended Term (the "Extension Rent Floor"),) Said Additional Term Extension Period shall commence, subject to proper exercise of Lessee's option hereunder, at the end of the Extended Term (i.e. on February 1, 2020) and shall terminate on that date which is sixty (60) consecutive months thereafter (i.e. January 31, 2025).

Lessee shall exercise its option by delivering to Lessor its written notice of said exercise not later than nine (9) full months (but not sooner than twelve (12) full months) prior to the end of the Extended Term. Once delivered, written notice to extend is irrevocable. Time is of the essence in the exercise of Lessee's rights as set forth above.

"Market Rent" as used herein, shall be that rent charged for comparable research laboratory and office space of similar age and condition in laboratory buildings the mid-Cambridge submarket as of the end of the Extended Term. If, after good faith attempts prior to the expiration of the original Term, the Lessor and Lessee cannot agree on a figure representing Market Rent, then either party, upon written notice to the other, may request appraisal and arbitration of the issue as provided in this section. Within fourteen (14) days of the request for arbitration, each party shall submit to the other the name of one unrelated individual or entity with proven expertise in the leasing of commercial real estate in Cambridge to serve as that party's appraiser. Each appraiser shall be paid by the party selecting him or it. The two appraisers shall each submit their final reports to the parties within thirty (30) days of their selection making their determination as to Market Rent (subject however, to the Extension Rent Floor). The two appraisers shall meet within the next fourteen (14) days to reconcile their reports and collaboratively determine the Market Rent. They shall each make their determination in writing (subject however, to the Extension Rent Floor), including a statement if such is the case, that they are at an impasse. Such a statement of impasse shall be submitted to the parties along with the Market Rent figure which each appraiser has selected and his reasons and substantiation therefor. The appraisers, in case of an impasse, shall also agree on one unrelated individual or entity with expertise in commercial real estate in Cambridge who shall evaluate the reports of the two original appraisers and, within fourteen (14) days of submission of the issue to him, make his own determination as to a figure representing Market Rent (subject however, to the Extension Rent Floor). The determination of this individual or entity (i.e. arbitrator) absent, fraud, bias or undue prejudice shall be binding upon the parties.

Annual Base Rent and Additional Rent during any Additional Term Extension Period shall be payable in advance, in equal monthly installments on the first day of each calendar month.

Lessee, in addition to the sums payable annually to Lessor as Annual Base Rent, shall pay to Lessor for each year of the Additional Term Extension Period, as Additional Rent, Lessee's Allocable Percentage for Operating Expenses, Real Estate Taxes and utilities as contemplated in Section 4 hereof.

9. Integration of Documents; Supremacy

This Second Amendment contains the full understanding and agreement between the parties with respect to the subject matter hereof. The parties hereto intend that this Second Amendment operates to amend and modify the Existing Lease in the manner stated herein, and that the Existing Lease and this Second Amendment shall be interpreted conjunctively; with any express conflict between the three to be resolved in favor of the stated terms of this Second Amendment. Except as modified hereby, all other terms and conditions of the Existing Lease shall remain unchanged and enforceable in a manner consistent with this Second Amendment.

This Agreement shall be governed by the laws of the Commonwealth of Massachusetts. Any provisions deemed unenforceable shall be severable, and the remainder of this Second Amendment and the Existing Lease shall be enforceable in accordance with their terms.

[Signature Pages Follow]

Executed as of the date first written above.

LESSOR

RIVERTECH ASSOCIATES II, LLC

By: /s/ David Epstein

its duly authorized Manager

LESSEE

DIMENSION THERAPEUTICS, INC.

By: /s/ Annalisa Jenkins MBBS, FRCP

its duly authorized President

By /s/ Jean Franchi

Its duly authorized Treasurer

Exhibit 31.1

CERTIFICATIONS

I, Annalisa Jenkins, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Dimension Therapeutics, 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(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

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

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

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

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

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

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

Date: August 8, 2017

By: /s/ Annalisa Jenkins
Annalisa Jenkins
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Mary Thistle, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Dimension Therapeutics, 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(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

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

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

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

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

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

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

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

Date: August 8, 2017

By: /s/ Mary Thistle
Mary Thistle
Chief Operating Officer
(Principal Financial Officer)

Exhibit 32.1

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

In connection with the Quarterly Report on Form 10-Q of Dimension Therapeutics, Inc. (the "Company") for the period ended June 30, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. Section 1350, that to her knowledge:

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

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

Date: August 8, 2017

By: /s/ Annalisa Jenkins
Annalisa Jenkins
President and Chief Executive Officer
(Principal Executive Officer)

Date: August 8, 2017

By: /s/ Mary Thistle
Mary Thistle
Chief Operating Officer
(Principal Financial Officer)