UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 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, 2016

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 001-32157

Mast Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**84-1318182**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
3611 Valley Centre Dr., Suite 500, San Diego, CA	**92130**
(Address of principal executive offices)	**(Zip Code)**

(858) 552-0866
(Registrant's telephone number, including area code)

N/A
(Former name, former address and former fiscal year, if changed since last report)

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 or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐	Smaller reporting company	☐

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 outstanding of the registrant's common stock, $0.001 par value per share, as of August 5, 2016 was 211,815,450.

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PART I — FINANCIAL INFORMATION

Item 1. Financial Statements

Mast Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Balance Sheets
(Unaudited)
(in thousands, except for share and par value data)

	June 30, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 24,490	$ 23,052
Investment securities	10,582	17,929
Prepaid expenses and other current assets	746	1,271
Total current assets	35,818	42,252
Property and equipment, net	171	226
In-process research and development	8,549	8,549
Goodwill	3,007	3,007
Other assets	131	183
Total assets	$ 47,676	$ 54,217
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,300	$ 2,600
Accrued liabilities	9,424	8,152
Accrued compensation and payroll taxes	1,127	1,430
Debt facility	12,512	10,991
Total current liabilities	25,363	23,173
Long-term lease obligation	21	25
Debt facility, net of current portion	2,462	3,726
Deferred income tax liability	3,404	3,404
Total liabilities	31,250	30,328
Stockholders' equity:		
Common stock, $0.001 par value; 500,000,000 shares authorized; 208,341,530 and 163,614,297 shares issued and outstanding at June 30, 2016 and December 31, 2015, respectively	208	164
Additional paid-in capital	313,097	298,715
Accumulated other comprehensive income/(loss)	7	(17)
Accumulated deficit	(296,886)	(274,973)
Total stockholders' equity	16,426	23,889
Total liabilities and stockholders' equity	$ 47,676	$ 54,217

See accompanying notes to unaudited condensed consolidated financial statements.

Mast Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Statements of Operations and Comprehensive Loss
(Unaudited)
(in thousands, except for share and per share data)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Revenues	$ —	$ —	$ —	$ —
Operating expenses:				
Research and development	7,752	7,734	15,627	13,776
Selling, general and administrative	2,439	2,410	5,274	5,988
Depreciation and amortization	30	37	61	67
Total operating expenses	10,221	10,181	20,962	19,831
Loss from operations	(10,221)	(10,181)	(20,962)	(19,831)
Interest income	36	32	75	62
Interest expense	(512)	(1)	(1,031)	(1)
Other income (loss), net	(9)	(1)	5	3
Net loss	$ (10,706)	$ (10,151)	$ (21,913)	$ (19,767)
Net loss per share - basic and diluted	$ (0.05)	$ (0.06)	$ (0.12)	$ (0.12)
Weighted average shares outstanding - basic and diluted	196,553,963	162,128,100	187,334,590	160,800,809
Comprehensive Income/(Loss):				
Net loss	$ (10,706)	$ (10,151)	$ (21,913)	$ (19,767)
Other comprehensive income	2	12	24	35
Comprehensive net loss	$ (10,704)	$ (10,139)	$ (21,889)	$ (19,732)

See accompanying notes to unaudited condensed consolidated financial statements.

Mast Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Statements of Cash Flows
(Unaudited)
(in thousands)

	Six Months Ended June 30,	
	2016	**2015**
Cash flows from operating activities:		
Net loss	$ (21,913)	$ (19,767)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	61	67
Share-based compensation expense related to employee stock options	1,306	1,578
Amortization of debt issuance costs and debt discount	332	—
Changes in assets and liabilities:		
Decrease/(increase) in prepaid expenses and other assets	577	(124)
Increase in accounts payable and accrued liabilities	668	2,364
Net cash used in operating activities	(18,969)	(15,882)
Cash flows from investing activities:		
Purchases of certificates of deposit	—	(7,986)
Proceeds from maturities of certificates of deposit	7,371	7,337
Purchases of property and equipment	(7)	(91)
Net cash provided by/(used in) investing activities	7,364	(740)
Cash flows from financing activities:		
Proceeds from sale of common stock	14,033	2,140
Payments for offering costs	(939)	(109)
Payments for capital lease	(4)	(3)
Costs paid in connection with debt facility	(47)	—
Net cash provided by financing activities	13,043	2,028
Net increase/(decrease) in cash and cash equivalents	1,438	(14,594)
Cash and cash equivalents at beginning of period	23,052	35,808
Cash and cash equivalents at end of period	$ 24,490	$ 21,214

See accompanying notes to unaudited condensed consolidated financial statements.

1. Basis of Presentation

Mast Therapeutics, Inc., a Delaware corporation ("Mast Therapeutics," "we" or "our company"), prepared the unaudited interim condensed consolidated financial statements included in this report in accordance with United States generally accepted accounting principles ("U.S. GAAP") for interim financial information and the rules and regulations of the Securities and Exchange Commission ("SEC") related to quarterly reports on Form 10-Q. Accordingly, they do not include all of the information and disclosures required by U.S. GAAP for annual audited financial statements and should be read in conjunction with our audited consolidated financial statements and notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2015, filed with the SEC on March 14, 2016 ("2015 Annual Report"). The condensed consolidated balance sheet as of December 31, 2015 included in this report has been derived from the audited consolidated financial statements included in the 2015 Annual Report. In the opinion of management, these condensed consolidated financial statements include all adjustments (consisting of normal recurring adjustments) necessary for a fair statement of the financial position, results of operations and cash flows for the periods presented. The results of operations for the interim periods shown in this report are not necessarily indicative of the results that may be expected for any future period, including the full year.

We are a biopharmaceutical company focused on developing clinical-stage therapies for serious or life-threatening diseases. We have devoted substantially all of our resources to research and development ("R&D") and acquisition of our product candidates. We have not yet marketed or sold any products or generated any significant revenue. Through our acquisition of SynthRx, Inc. ("SynthRx") in 2011, we acquired our Membrane Adhesion & Sealant Technology (MAST) platform, which includes proprietary poloxamer-related data and know-how derived from over two decades of clinical, nonclinical and manufacturing experience, and we are leveraging the MAST platform to develop vepoloxamer (also known as MST-188) for serious or life-threatening diseases and conditions typically characterized by impaired microvascular blood flow and damaged cell membranes. Through our acquisition of Aires Pharmaceuticals, Inc. ("Aires") in February 2014, we acquired AIR001, a sodium nitrite inhalation solution for intermittent inhalation via nebulization, which we are developing for the treatment of heart failure with preserved ejection fraction (HFpEF).

The accompanying condensed consolidated financial statements have been prepared assuming we will continue to operate as a going concern, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. However, our working capital, anticipated operating expenses and net losses and the uncertainties surrounding our ability to raise additional capital as needed, as discussed below, raise substantial doubt about our ability to continue as a going concern. The accompanying condensed consolidated financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts of liabilities that may result from uncertainty related to our ability to continue as a going concern.

We have incurred significant operating losses since inception and have relied on our ability to fund our operations primarily though equity financings and a debt financing. For the year ended December 31, 2015 and the six months ended June 30, 2016, we incurred losses from operations of $39.4 million and $21.0 million, respectively, and our net cash used in operating activities was $32.9 million and $19.0 million, respectively. At June 30, 2016, our cash, cash equivalents and investment securities totaled $35.1 million and our working capital was $10.5 million. Our planned operating activities call for expenditures over the next 12 months to exceed our current cash, cash equivalents and investment securities balances and working capital. We intend to raise additional capital this year through our "at the market," or ATM, equity offering program (See Note 13, "Stockholders' Equity"), other equity or debt financings, and/or through collaborations, including licensing agreements. There can be no assurance that we will be successful in raising sufficient additional capital or that such capital, if available, will be on terms that are acceptable to us. Subject to limited exceptions, our debt facility (See Note 8, "Debt Facility") prohibits us from incurring indebtedness without the lender's prior written consent. Our anticipated operating expenses and net losses and the uncertainties surrounding our ability to raise additional capital as needed raise substantial doubt about our ability to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and might realize significantly less than the values at which they are carried on our financial statements. If we are unable to raise sufficient additional capital this year, we intend to significantly reduce the scope of our planned operations during the fourth quarter, including by delaying or discontinuing investment in development and commercial-readiness activities for vepoloxamer in sickle cell disease and heart failure, even if we have positive results from our Phase 3 clinical study of vepoloxamer in sickle cell disease, known as the EPIC study. In the event of negative results from the EPIC study and/or prepayment to our lender on or before October 14, 2016 of $10.0 million of the principal balance under our debt facility in accordance with its terms, we plan to immediately and more drastically reduce the scope of our operations. In either case, we expect that our cash, cash equivalents and investment securities as of June 30, 2016, would be sufficient to fund our operations, as reduced in scope, into the first quarter of 2017.

In addition to the uncertainties surrounding our ability to raise additional capital as needed which raise substantial doubt about our ability to continue as a going concern, our business, operating results, financial condition, and growth prospects are subject

to significant other risks and uncertainties, including failing to complete development of and obtain regulatory approval to commercialize our product candidates even if we are able to raise significant additional capital.

2. Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in our consolidated financial statements and accompanying notes. On an ongoing basis, we evaluate our estimates and assumptions, including estimates related to R&D expenses, in-process research and development ("IPR&D"), goodwill, and share-based compensation expenses. We base our estimates on historical experience and various other relevant assumptions we believe to be reasonable under the circumstances. Actual results may differ from these estimates.

3. Goodwill and IPR&D

At June 30, 2016 and December 31, 2015, our goodwill and IPR&D consisted of the following (in thousands):

Goodwill	$	3,007
IPR&D		
Acquired IPR&D related to SynthRx acquisition		6,549
Acquired IPR&D related to Aires acquisition		2,000
Total goodwill and IPR&D	$	11,556

Our goodwill represents the difference between the total purchase price for SynthRx and the aggregate fair values of tangible and intangible assets acquired, less liabilities assumed.

Our IPR&D consists of the estimated fair values of the vepoloxamer and AIR001 programs as of the dates we acquired SynthRx and Aires, respectively.

We test our goodwill and acquired IPR&D for impairment annually as of September 30, or, in the case of initially acquired IPR&D, on the first anniversary of the date we acquired it and subsequently on September 30, and between annual tests if we become aware of an event or a change in circumstances that would indicate the carrying value may be impaired. We performed a qualitative assessment of our goodwill and our acquired IPR&D as of September 30, 2015. We concluded that it is not more likely than not that the carrying value of our goodwill or our acquired IPR&D exceeds its fair value. Therefore, we concluded that no impairment charge is required.

4. Investment Securities

Investment securities are marketable equity or debt securities. All of our investment securities are "available-for-sale" securities and carried at fair value. Fair value for securities with short maturities and infrequent secondary market trades typically is determined by using a curve-based evaluation model that utilizes quoted prices for similar securities. The evaluation model takes into consideration the days to maturity, coupon rate and settlement date convention. Net unrealized gains or losses on these securities are included in accumulated other comprehensive loss, which is a separate component of stockholders' equity. Realized gains and realized losses are included in other income, net while amortization of premiums and accretion of discounts are included in interest income. Interest and dividends on available-for-sale securities are included in interest income. We periodically evaluate our investment securities for impairment. If we determine that a decline in fair value of any investment security is other than temporary, then the cost basis would be written down to fair value and the decline in value would be charged to earnings.

Our investment securities are under the custodianship of a major financial institution and consist of FDIC-insured certificates of deposit. We have classified all of our available-for-sale investment securities, as current assets on our consolidated balance sheets because we consider them to be highly liquid and available for use, if needed, in current operations. As of June 30, 2016, none of our investment securities had contractual maturity dates of more than one year.

At June 30, 2016 and December 31, 2015, our investment securities were as follows (in thousands):

	June 30, 2016	December 31, 2015
Fair value of investment securities	$ 10,582	$ 17,929
Cost basis of investment securities	10,575	17,946

	June 30, 2016	December 31, 2015
Net unrealized (gains)/losses on investment securities	$ (7)	$ 17

5. Fair Value of Financial Instruments

Our cash equivalents are recorded at cost plus accrued interest, which approximates fair value. Our investment securities are carried at fair value. The fair value of financial assets and liabilities is measured under a framework that establishes "levels" which are defined as follows: (i) Level 1 fair value is determined from observable, quoted prices in active markets for identical assets or liabilities; (ii) Level 2 fair value is determined from inputs, other than Level 1 inputs, that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities, and (iii) Level 3 fair value is determined using the entity's own assumptions about the inputs that market participants would use in pricing an asset or liability.

The fair values at June 30, 2016 and December 31, 2015 of our cash equivalents and investment securities are summarized in the following table (in thousands):

		Fair Value Determined Under:		
	Total Fair Value	(Level 1)	(Level 2)	(Level 3)
At June 30, 2016:				
Cash equivalents	$ 13,234	$ 13,234	$ —	$ —
Investment securities	$ 10,582	$ —	$ 10,582	$ —
At December 31, 2015:				
Cash equivalents	$ 15,799	$ 15,799	$ —	$ —
Investment securities	$ 17,929	$ —	$ 17,929	$ —

We believe that our debt facility (see Note 8 "Debt Facility") bears interest at a rate that approximates prevailing market rates for instruments with similar characteristics and, accordingly, the carrying value of the debt facility approximates fair value. The fair value of our debt facility is determined under Level 2 in the fair value hierarchy.

6. Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation and amortization. Property and equipment are depreciated using the straight-line method over the estimated useful lives of the assets, which generally is three to five years. Leasehold improvements are amortized over the economic life of the asset or the lease term, whichever is shorter. Repairs and maintenance are expensed as incurred.

We lease certain office equipment under leases classified as capital leases. As of June 30, 2016, the total amount of leased equipment was $40,000 with interest rates ranging from 8% to 14% per annum. The equipment is being amortized over the life of the leases, which range from three to five years.

7. Accrued Liabilities

Accrued liabilities at June 30, 2016 and December 31, 2015 were as follows (in thousands):

	June 30, 2016	December 31, 2015
Accrued R&D agreements and study expenses	$ 8,401	$ 7,898
Obligation to provide common stock	686	-
Other accrued liabilities	337	254
Total accrued liabilities	$ 9,424	$ 8,152

Under our ATM program (See Note 13, "Stockholders' Equity"), we received cash on June 30, 2016 from our sales agent in payment of shares of our common stock sold in June, but the shares were not issued by the registrar and transfer agent for our common stock until July 1, 2016. Accordingly, we recorded a current liability for the cash received for the shares that were issued on July 1, 2016.

8. Debt Facility

Hercules Loan and Security Agreement

We have borrowed an aggregate of $15.0 million pursuant to a Loan and Security Agreement, dated August 11, 2015, with Hercules Technology III, L.P. and Hercules Capital, Inc. (formerly known as, Hercules Technology Growth Capital, Inc.)

(together, "Hercules"), as amended by the First Amendment thereto dated September 28, 2015, the Second Amendment thereto dated December 31, 2015, the Third Amendment thereto dated February 25, 2016, and the Fourth Amendment thereto dated July 22, 2016 (collectively, the "Loan Agreement"). Pursuant to the terms and conditions of the Loan Agreement, we received the first advance of $5.0 million on August 11, 2015 and the second advance of $10.0 million on September 28, 2015.

Under the Loan Agreement, we are required to prepay to Hercules $10 million of the principal balance of the loan and any accrued but unpaid fees and expenses (the "Second Advance Prepayment") on or before October 14, 2016 unless on or before such date, we demonstrate, to the reasonable satisfaction of Hercules, positive results in our Phase 3 clinical study of vepoloxamer in patients with sickle cell disease, known as the EPIC study (the "Second Advance Prepayment Condition"). In the event that the Second Advance Prepayment Condition is not satisfied, the Second Advance Prepayment would be due on October 14, 2016; provided, however, that if we issue a public announcement of EPIC results that do not satisfy the Second Advance Prepayment Condition before October 14, 2016, we are required to make the Second Advance Prepayment promptly, but in any case, within three business days of the public announcement. Due to numerous factors, we are not able to predict with any reasonable certainty the probability of achieving the Second Advance Prepayment Condition; therefore, we have classified the Second Advance as a current liability on the balance sheet.

The interest rate for the principal balance under the Loan Agreement is the greater of (i) 8.95% plus the prime rate as reported in The Wall Street Journal minus 3.25%, and (ii) 8.95%, determined on a daily basis. Monthly payments under the Loan Agreement were interest only until July 1, 2016. Beginning July 1, 2016 and on the first business day of each month thereafter through the scheduled maturity date of January 1, 2019, we will repay the principal balance under the Loan Agreement in equal monthly installments of principal and interest. However, if we achieve the Second Advance Prepayment Condition, we have not made the Second Advance Prepayment, and no event of default has occurred, we can resume making interest-only payments and further payments against the principal balance will be deferred until March 1, 2017. If our interest-only payment period resumes and is extended to March 1, 2017, then the maturity date would extend to October 1, 2019. An end of term charge of $712,500 will be due on the scheduled maturity date and is being accrued through interest expense using the effective interest method.

If we elect to prepay the principal balance under the Loan Agreement prior to maturity, a prepayment charge of 1%, 2% or 3%, of the then outstanding principal balance also will be due, depending upon when the prepayment occurs. No prepayment penalty would apply to the Second Advance Prepayment, if required.

Our obligations under the Loan Agreement are secured by a first priority security interest in substantially all of our assets, excluding our intellectual property but including the proceeds from the sale, licensing or disposition of our intellectual property. Our intellectual property is subject to customary negative covenants.

In connection with the Loan Agreement, we have paid facility charges of $225,000 and a commitment charge of $25,000. Such charges were accounted for as debt issuance costs and are being amortized to interest expense using the effective interest method through the scheduled maturity date.

In connection with the Loan Agreement, we entered into a Warrant Agreement with Hercules, dated August 11, 2015, as amended by the First Amendment thereto dated September 28, 2015 and the Second Amendment thereto dated February 25, 2016, pursuant to which Hercules has a right to purchase up to 2,272,727 shares of our common stock at an exercise price of $0.275 per share. Prior to the Second Amendment to Warrant Agreement, the Warrant Agreement, as amended by the First Amendment, provided Hercules a right to purchase up to 1,524,390 shares of our common stock at an exercise price of $0.41 per share.

The warrants issued to Hercules were valued using the Black-Scholes option pricing model with the following assumptions: volatility of 83%, expected term of five years, risk-free interest rate of 1.2% and a zero dividend yield. The warrant fair value of $0.4 million has been recorded as a debt discount and is being amortized through interest expense using the effective interest method through the scheduled maturity date. See Note 13 "Stockholders' Equity" for further description of the terms of the warrants.

Summary of Carrying Value

The following table summarizes the components of the debt facility carrying value (in thousands):

	As of June 30, 2016	
	Short-term	Long-term
Potential prepayment to lender	$ 10,000	$ -
Principal payments to lender and end of term charge	2,397	3,316
Accrued interest	115	-
Debt issuance costs	-	(594)
Debt discount related to warrants	-	(260)
Carrying value	$ 12,512	$ 2,462

9. Share-Based Compensation Expense

Share-based compensation expense related to equity awards granted to our employees and non-employee directors for the three and six months ended June 30, 2016 and 2015 was as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Selling, general and administrative expense	$ 425	$ 371	$ 849	$ 1,312
Research and development expense	222	141	457	266
Share-based compensation expense	$ 647	$ 512	$ 1,306	$ 1,578

During the six months ended June 30, 2016, the only equity awards granted to our employees and non-employee directors were stock option awards. The following table summarizes the equity award activity during such six-month period:

	Shares Underlying Option Awards	Weighted-Average Exercise Price
Outstanding at December 31, 2015	22,896,728	$ 0.78
Granted	8,151,263	$ 0.42
Exercised	—	$ —
Expired/forfeited	(1,012,106)	$ 0.90
Outstanding at June 30, 2016	30,035,885	$ 0.68

At June 30, 2016, total unrecognized estimated compensation cost related to non-vested employee and non-employee director share-based awards granted prior to that date was $5.3 million, which is expected to be recognized over a weighted-average period of 2.7 years.

10. Net Loss Per Common Share

Basic and diluted net loss per common share was calculated by dividing the net loss for the three and six months ended June 30, 2016 and 2015 by the weighted-average number of common shares outstanding during those periods, respectively, without consideration for outstanding common stock equivalents because their effect would have been anti-dilutive. Common stock equivalents are included in the calculation of diluted earnings per common share only if their effect is dilutive. For the periods presented, our outstanding common stock equivalents consisted of options and warrants to purchase shares of our common stock. All common stock equivalents presented had an anti-dilutive impact due to losses reported in the applicable periods. The weighted-average number of those common stock equivalents outstanding for each of the periods presented is set forth in the table below:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Options	30,029,718	20,148,555	30,176,166	20,454,379
Warrants	105,178,730	76,559,927	97,712,362	77,847,594

11. Recent Accounting Pronouncements

In March 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2016-09, *Compensation – Stock Compensation* ("ASU 2016-09"), which involves multiple aspects of the accounting for share-based transactions, including income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. For public companies, ASU 2016-09 is effective for fiscal years beginning after December 15, 2016, including interim periods within those fiscal years. Early adoption is permitted. We are in the process of evaluating the impact of this new guidance.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (ASC 842)* ("ASU 2016-02"), ASU 2016-02 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 classify 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. Accounting Standards Codification ("ASC") 842 supersedes the previous leases standard, ASC 840 *Leases*. The standard is effective on January 1, 2019, with early adoption permitted. We are in the process of evaluating the impact of this new guidance.

In November 2015, the FASB issued ASU No. 2015-17, *Balance Sheet Classification of Deferred Taxes* ("ASU 2015-17"). Currently deferred taxes for each tax jurisdiction are presented as a net current asset or liability and net noncurrent asset or liability on the balance sheet. To simplify the presentation, the new guidance requires that all deferred tax assets and liabilities for each jurisdiction, along with any related valuation allowance, be classified as noncurrent on the balance sheet. The new guidance becomes effective for public business entities in fiscal years beginning after December 15, 2016. We elected to early adopt this new standard prospectively for the year ended December 31, 2015 and it did not have a material impact on our financial statements.

In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements - Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern* ("ASU 2014-15"). The amendments in ASU 2014-15 will require management to assess, at each annual and interim reporting period, the entity's ability to continue as a going concern and, if management identifies conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued, to disclose in the notes to the entity's financial statements the principal conditions or events that raised substantial doubt about the entity's ability to continue as a going concern, management's evaluation of their significance, and management's plans that alleviated or are intended to alleviate substantial doubt about the entity's ability to continue as a going concern. ASU 2014-15 is effective for annual periods ending after December 15, 2016 and early application is permitted. The amendments in ASU 2014-15 do not have any application to an entity's financial statements, but only to the related notes.

12. Supplemental Cash Flow Information

Non-cash investing and financing transactions presented separately from the condensed consolidated statements of cash flows for the six months ended June 30, 2016 and 2015 are as follows (in thousands):

	Six Months Ended June 30,	
	2016	2015
Cash paid for interest on debt facility	$ 700	$ -
Supplemental disclosures of non-cash investing and financing activities:		
Warrants issued in connection with debt facility	$ 26	$ -
Unrealized gain on investment securities	$ (24)	$ (35)

13. Stockholders' Equity

Underwritten Public Offering of Common Stock and Warrants

In February 2016, we completed an underwritten public offering with gross proceeds of $8.0 million from the sale and issuance of 29,090,910 units, each consisting of one share of our common stock and one warrant to purchase one share of our common stock. Net proceeds, after deducting underwriting discounts and commissions and other estimated offering expenses, were

approximately $7.3 million. The warrants have an exercise price of $0.42 per share, are exercisable any time on or after August 17, 2016 and will expire on February 16, 2021.

"At the Market" Equity Offering Program

In February 2014, we entered into a sales agreement with Cowen and Company, LLC ("Cowen"), to sell shares of our common stock, with aggregate gross sales proceeds of up to $30.0 million, from time to time, through an "at the market," or ATM, equity offering program (the "2014 Sales Agreement"), under which Cowen acted as sales agent. In August 2015, we terminated the 2014 Sales Agreement upon entry into a new sales agreement with Cowen to sell shares of our common stock, with aggregate gross sales proceeds of up to $30.0 million, from time to time, through an ATM program. As of June 30, 2016, we had sold an aggregate of 42,015,010 shares at a weighted-average sales price of $0.58 per share under the ATM programs for aggregate gross proceeds of $24.2 million and $23.1 million in net proceeds, after deducting sales agent commission and discounts and our other offering costs. As of June 30, 2016, 40,495,430 of the 42,015,010 shares sold had been issued; the remaining 1,519,580 shares sold were issued on July 1, 2016.

Shares Issuable to Former SynthRx Stockholders Upon Achievement of Milestones

In April 2011, we acquired SynthRx as a wholly-owned subsidiary through a merger transaction in exchange for shares of our common stock and rights to additional shares of our common stock upon achievement of specified milestones related to the development of MST-188 in sickle cell disease. We have issued an aggregate of 3,050,851 shares of our common stock to the former SynthRx stockholders, 1,454,079 of which we repurchased in December 2012 for $0.001 per share pursuant to our exercise of a repurchase right under the merger agreement. We could issue up to an aggregate of 12,478,050 additional shares of our common stock to the former SynthRx stockholders if and when the development of MST-188 achieves the following milestones: (a) 3,839,400 shares upon acceptance for review by the U.S. Food and Drug Administration ("FDA") of a new drug application ("NDA") covering the use of purified poloxamer 188 for the treatment of sickle cell crisis in children and (b) 8,638,650 shares upon approval of such NDA by the FDA.

Warrants Issued to Hercules

In connection with the Loan Agreement, we entered into a Warrant Agreement with Hercules Technology III, L.P., dated August 11, 2015, as amended by the First Amendment thereto dated September 28, 2015 and the Second Amendment thereto dated February 25, 2016, pursuant to which Hercules has a right to purchase up to an aggregate of 2,272,727 shares of our common stock at an exercise price of $0.275 per share, at any time, or from time to time, through August 11, 2020. The Warrant Agreement, as amended, provides for adjustment to the exercise price and number of shares subject to Hercules' warrants in the event of a merger event, reclassification of our common stock, subdivision or combination of our common stock, or certain dividend payments. Upon exercise, the aggregate exercise price may be paid, at Hercules' election, in cash or on a net issuance basis, based upon the fair market value of our common stock at the time of exercise. If the fair market value of our common stock is greater than the exercise price of the warrants as of immediately before their expiration, to the extent the warrants are not previously exercised in full, the warrants shall be deemed automatically exercised on a net issuance basis as of immediately before their expiration.

Outstanding Warrants

At June 30, 2016, outstanding warrants to purchase shares of common stock are as follows:

Shares Underlying Outstanding Warrants		Exercise Price	Expiration Date
10,625,000	$	1.100	November 2016
28,097,400	$	0.650	June 2018
13,081,428	$	0.010	November 2019
22,011,265	$	0.750	November 2019
2,272,727	$	0.275	August 2020
29,090,910	$	0.420	February 2021
105,178,730			

14. Subsequent Events

Amendment to Loan and Security Agreement

In July 2016, we entered into that certain Fourth Amendment to Loan and Security Agreement with Hercules (the "Fourth Amendment"), primarily to extend a key date relating to our conditional obligation to prepay $10 million of the principal

balance of the loan and to provide for deferral of further payments against the principal balance until March 1, 2017 and extension of the scheduled maturity date to October 1, 2019 if that $10 million prepayment is not required and no event of default has occurred.

As described in Note 8 “Debt Facility,” in the event that the Second Advance Prepayment Condition is not satisfied, the Second Advance Prepayment would be due on October 14, 2016; provided, however, that if we issue a public announcement of EPIC results that do not satisfy the Second Advance Prepayment Condition before October 14, 2016, we are required to make the Second Advance Prepayment promptly, but in any case, within three business days of the public announcement. If the Second Advance Prepayment Condition is satisfied, we are not required to make the Second Advance Prepayment, and no event of default under the Loan Agreement has occurred, we can resume making interest-only payments to Hercules and further payments against the principal balance will be deferred until March 1, 2017. If the interest-only payment period resumes, the scheduled maturity date of the loan would extend from January 1, 2019 to October 1, 2019. Pursuant to the Fourth Amendment we paid an additional facility charge of $75,000.

Shares Issued under ATM Program

As described above under Note 7 “Accrued Liabilities” and Note 13 “Stockholders’ Equity,” in June 2016, we received payment from Cowen, the sales agent for our ATM program, for 1,519,580 shares of our common stock sold under our ATM program, but we did not issue those shares until July 1, 2016. As a result, at June 30, 2016, we recorded a current liability to provide the 1,519,580 shares that had been sold and paid for, but not yet issued.

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with the condensed consolidated financial statements and accompanying notes appearing elsewhere in this report. For additional context with which to understand our financial condition and results of operations, see the discussion and analysis included in Part II, Item 7 of our annual report on Form 10-K for the year ended December 31, 2015, filed with the U.S. Securities and Exchange Commission, or SEC, on March 14, 2016, as well as the consolidated financial statements and accompanying notes contained therein. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties, and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of various factors, including but not limited to those identified under "Forward Looking Statements" below and those discussed in Item 1A (Risk Factors) of Part II of this report. Mast Therapeutics, our corporate logo, Aires Pharmaceuticals, Inc., VOICE Crisis Alert, and SynthRx are trademarks of our company. All trademarks, service marks or trade names appearing in this report are the property of their respective owners. Use or display by us of other parties' trademarks, service marks or trade names is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark, service mark or trade name owners.

Overview

We are a biopharmaceutical company developing clinical-stage therapies for serious or life-threatening diseases with significant unmet needs and we currently are focused on developing new therapies for sickle cell disease and heart failure. Our lead product candidate, vepoloxamer (also known as MST-188), is in Phase 3 clinical development for sickle cell disease and Phase 2 clinical development for heart failure with reduced ejection fraction. We are leveraging our Molecular Adhesion & Sealant Technology, or MAST, platform, derived from over two decades of clinical, nonclinical, and manufacturing experience with purified and non-purified poloxamers, to develop vepoloxamer, which has demonstrated multiple pharmacologic effects that may provide clinical benefit in a wide range of diseases and conditions typically characterized by impaired microvascular blood flow and/or damaged cell membranes. Our second product candidate, AIR001, a sodium nitrite solution for inhalation via nebulization, has demonstrated positive hemodynamic benefits in patients with heart failure with preserved ejection fraction, or HFpEF, and pulmonary hypertension, and currently is in Phase 2 clinical development for HFpEF.

We have devoted substantially all of our resources to research and development, or R&D, and to acquisition of our product candidates. We have not yet marketed or sold any products or generated any significant revenue and we have incurred significant annual operating losses since inception. We incurred a loss from operations of $21.0 million for the six months ended June 30, 2016. As of June 30, 2016, we had an accumulated deficit of $296.9 million. Our cash, cash equivalents, and investment securities were $35.1 million and our working capital was $10.5 million as of June 30, 2016.

As discussed below under "Management Outlook," we do not believe our cash, cash equivalents and investment securities as of June 30, 2016 will be sufficient to meet our currently planned operations for the next 12 months, and these circumstances raise substantial doubt about our ability to continue as a going concern.

Our development efforts have been funded primarily through the offering and sale of our equity securities from time to time and a debt facility under which we have a principal balance of $14.1 million as of August 5, 2016. The process of developing and seeking regulatory approval for investigational new drug products and marketing such products, if approved, requires significant capital investment. We expect to continue to incur substantial operating losses for the next several years as we advance our product candidates through clinical development and, if successful, seek regulatory approval to market and sell them. Until such time as we obtain regulatory approval and are subsequently able to generate positive cash flow, we plan to continue to fund our operations with our current cash, cash equivalents and investment securities and by raising additional capital through our "at the market," or ATM, equity offering program, other equity or debt financings, and/or through collaborations, including licensing arrangements. If we are not successful in raising sufficient additional capital as needed, we may be compelled to reduce the scope of our operations and planned capital expenditures and/or sell or license certain assets at inopportune times, which could have a material and adverse effect on our ability to pursue our business strategy. We have already implemented cost-saving measures, including with respect to our vepoloxamer programs, except in regard to completing database lock and obtaining results from our Phase 3 clinical study of vepoloxamer in sickle cell disease, known as the EPIC study. If we are unable to raise sufficient additional capital this year, we plan to further reduce the scope of our operations during the fourth quarter, including by further delaying or discontinuing investment in development and commercial-readiness activities for vepoloxamer in sickle cell disease and heart failure, even if we have positive results from the EPIC study. In the event of negative results from the EPIC study and/or prepayment to our lender on or before October 14, 2016 of $10 million of the principal balance under our debt facility, as would be required by its terms, we plan to immediately and more drastically reduce the scope of our operations.

We completed enrollment in the EPIC study earlier this year, and we expect to report top-line data in September 2016. Vepoloxamer also is currently being evaluated in a randomized, double-blind, placebo-controlled, multicenter Phase 2 study in patients with chronic heart failure. In addition, we continue to evaluate the opportunity for clinical development of vepoloxamer in ischemic stroke and our vepoloxamer pipeline includes a preclinical development program in resuscitation following major trauma (i.e., restoration of

circulating blood volume and pressure). We obtained the MAST platform and vepoloxamer program through our acquisition of SynthRx, Inc. in April 2011.

Our second product candidate, AIR001, is in Phase 2 clinical development for HFpEF. In February 2016, we announced positive top-line results from a 30-patient, randomized, double-blind, placebo-controlled Phase 2a study of AIR001 in patients with HFpEF. The study met its pre-specified primary endpoint, with the AIR001 treatment group showing a statistically significant decrease in pulmonary capillary wedge pressure during exercise compared to the control group and AIR001 was generally well-tolerated. Another institution-sponsored Phase 2a clinical study of AIR001 in patients with HFpEF is ongoing. Positive interim results from that study were presented at a scientific conference in May 2016. In addition, we are supporting a randomized, double-blind, placebo-controlled crossover Phase 2 study of AIR001 in approximately 100 patients with HFpEF. The study, which is known as the Inorganic Nitrite Delivery to Improve Exercise Capacity in HFpEF (INDIE-HFpEF) study, is sponsored by Duke Clinical Research Institute as the Coordinating Center for the Heart Failure Clinical Research Network (HFN) and will be conducted at approximately 20 clinical centers in the U.S. that are part of the HFN. The first patient was dosed in July 2016. We obtained the AIR001 program through our acquisition of Aires Pharmaceuticals, Inc. in February 2014.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations included in this report is based upon consolidated financial statements and condensed consolidated financial statements that we have prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP. The preparation of these financial statements requires us to make a number of estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses in these financial statements and accompanying notes. On an ongoing basis, we evaluate these estimates and assumptions, including those related to determination of the fair value of goodwill and acquired in-process research and development, or IPR&D, and recognition of R&D expenses and share-based compensation. We base our estimates on historical information, when available, and assumptions believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities not readily apparent from other sources. Actual results may differ materially from these estimates under different assumptions or conditions.

We believe the following accounting estimates are those that can have a material impact on our financial condition or operating performance and involve substantial subjectivity and judgment in the application of our accounting policies to account for highly uncertain matters or the susceptibility of such matters to change. The following is not intended to be a comprehensive discussion of all of our significant accounting policies. See the notes accompanying our consolidated financial statements appearing in our most recent annual report on Form 10-K for a summary of all of our significant accounting policies and other disclosures required by U.S. GAAP.

Accrued Research and Development Expenses. As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. Many of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments, if necessary. The majority of our accrued expenses relate to R&D services and related expenses. Examples of estimated accrued R&D expenses include:

- fees paid to contract research organizations, or CROs, in connection with clinical studies;
- fees paid to investigative sites and investigators in connection with clinical studies;
- fees paid to contract manufacturing organizations, or CMOs, in connection with process development activities and production of nonclinical and clinical trial material;
- fees paid to vendors in connection with nonclinical development activities; and
- fees paid to consultants for regulatory-related advisory and data management services.

We base our accrued expenses related to CROs and CMOs on our estimates of the services received and efforts expended pursuant to purchase orders or contracts with multiple service providers that we engage to conduct and manage our clinical studies and manufacture our clinical trial material on our behalf. The financial terms of our arrangements with our CROs and CMOs are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful completion of specified process development activities or the successful enrollment of patients and the completion of clinical study milestones. In accruing these service fees, we estimate, as applicable, the time period over which services will be performed (e.g., enrollment of patients, activation of clinical sites, etc.). If the actual timing varies from our estimate, we adjust the accrual accordingly. In addition, there may be instances in which payments made to service providers will exceed the level of services provided and result in a prepayment of R&D expense, which we report as an asset. The actual costs and timing of

clinical studies and research-related manufacturing are uncertain and subject to change depending on a number of factors. Differences between actual costs of these services and the estimated costs that we have accrued in a prior period are recorded in the subsequent period in which the actual costs become known to us. Historically, these differences have not resulted in material adjustments, but such differences may occur in the future and have a material impact on our consolidated results of operations or financial position.

Business Combinations. We account for business combinations, such as our acquisitions of SynthRx in April 2011 and Aires Pharmaceuticals in February 2014, in accordance with Accounting Standards Codification, or ASC, Topic 805, *Business Combinations*, which requires the purchase price to be measured at fair value. When the purchase consideration consists entirely of shares of our common stock, we calculate the purchase price by determining the fair value, as of the acquisition date, of shares issued in connection with the closing of the acquisition and, if the transaction involves contingent consideration based on achievement of milestones or earn-out events, the probability-weighted fair value, as of the acquisition date, of shares issuable upon the occurrence of future events or conditions pursuant to the terms of the agreement governing the business combination. If the transaction involves such contingent consideration, our calculation of the purchase price involves probability inputs that are highly judgmental due to the inherent unpredictability of drug development, particularly by development-stage companies such as ours. We recognize estimated fair values of the tangible assets and intangible assets acquired, including IPR&D, and liabilities assumed as of the acquisition date, and we record as goodwill any amount of the fair value of the tangible and intangible assets acquired and liabilities assumed in excess of the purchase price.

Goodwill and Acquired IPR&D. In accordance with ASC Topic 350, *Intangibles – Goodwill and Other*, or ASC Topic 350, our goodwill and acquired IPR&D are determined to have indefinite lives and, therefore, are not amortized. Instead, they are tested for impairment annually and between annual tests if we become aware of an event or a change in circumstances that would indicate the carrying value may be impaired. We perform our annual impairment testing as of September 30 of each year, or, in the case of initially acquired IPR&D, on the first anniversary of the date we acquired it and subsequently on September 30. Pursuant to Accounting Standards Update, or ASU, No. 2011-08, *Intangibles – Goodwill and Other (Topic 350): Testing Goodwill for Impairment*, and No. 2012-02, *Intangibles – Goodwill and Other (Topic 350): Testing Indefinite-Lived Intangible Assets for Impairment*, we have the option to first assess qualitative factors to determine whether the existence of events or circumstances leads us to determine that it is more likely than not (that is, a likelihood of more than 50%) that our goodwill or our acquired IPR&D is impaired. If we choose to first assess qualitative factors and we determine that it is not more likely than not that goodwill or acquired IPR&D is impaired, we are not required to take further action to test for impairment. We also have the option to bypass the qualitative assessment and perform only the quantitative impairment test, which we may choose to do in some periods but not in others.

If we perform a quantitative assessment of goodwill, we utilize the two-step approach prescribed under ASC Topic 350. Step 1 requires a comparison of the carrying value of a reporting unit, including goodwill, to its estimated fair value. We test for impairment at the entity level because we operate on the basis of a single reporting unit. If our carrying value exceeds our fair value, we then perform Step 2 to measure the amount of impairment loss, if any. In Step 2, we estimate the fair value of our individual assets, including identifiable intangible assets, and liabilities to determine the implied fair value of goodwill. We then compare the carrying value of our goodwill to its implied fair value. The excess of the carrying value of goodwill over its implied fair value, if any, is recorded as an impairment charge.

If we perform a quantitative assessment of IPR&D, we calculate the estimated fair value of acquired IPR&D by using the Multi-Period Excess Earnings Method, or MPEEM, which is a form of the income approach. Under the MPEEM, the fair value of an intangible asset is equal to the present value of the asset's projected incremental after-tax cash flows (excess earnings) remaining after deducting the market rates of return on the estimated value of contributory assets (contributory charge) over its remaining useful life.

Our determinations as to whether, and, if so, the extent to which, goodwill and acquired IPR&D become impaired are highly judgmental and based on significant assumptions regarding our projected future financial condition and operating results, changes in the manner of our use of the acquired assets, development of our acquired assets or our overall business strategy, and regulatory, market and economic environment and trends.

Share-based Compensation Expenses. We account for share-based compensation awards granted to employees, including non-employee members of our board of directors, in accordance with ASC Topic 718, *Compensation — Stock Compensation*. Compensation expense for all share-based awards is based on the estimated fair value of the award on its date of grant and recognized on a straight-line basis over its vesting period. As share-based compensation expense is based on awards ultimately expected to vest, it is reduced for estimated forfeitures. We estimate forfeitures at the time of grant based on the expected forfeiture rate for our unvested stock options, which is based in large part on our historical forfeiture rates, but also on assumptions believed to be reasonable under the circumstances. We revise our estimates in subsequent periods if actual forfeitures differ from those estimates. Although share-based compensation expense can be significant to our consolidated financial statements, it does not involve the payment of any cash by us.

We estimate the grant date fair value of a stock option award using the Black-Scholes option-pricing model, or Black-Scholes model. In determining the grant date fair value of a stock option award under the Black-Scholes model, we must make a number of

assumptions, including the term of the award, the volatility of the price of our common stock over the term of the award, and the risk-free interest rate. Changes in these or other assumptions could have a material impact on the compensation expense we recognize.

Results of Operations – Overview

We operate our business and evaluate our company on the basis of a single reportable segment, which is the business of developing therapies for serious or life-threatening diseases.

Revenue

We have not generated any revenue from product sales to date, and we do not expect to generate revenue from product sales until such time, if any, that we have obtained approval from a regulatory agency to sell one or more of our product candidates, which we cannot predict with certainty will occur. If we enter into any licensing or other collaborative arrangements regarding our development programs, we may recognize revenue from those arrangements prior to commercial sale of any products.

Operating Expenses

Research and Development Expenses. We maintain and evaluate our R&D expenses by the type of cost incurred rather than by project. We do this primarily because we outsource a substantial portion of our work and our R&D personnel and consultants work across multiple programs rather than dedicating their time to one particular program. We categorize our R&D expenses as external clinical study fees and expenses, external nonclinical study fees and expenses, personnel costs and share-based compensation expense. The major components of our external clinical study fees and expenses are fees and expenses related to CROs and clinical study investigative sites and investigators. The major components of our external nonclinical study fees and expenses are fees and expenses related to preclinical studies and other nonclinical testing, research-related manufacturing, quality assurance and regulatory affairs services, and preparation of a new drug application, or NDA, for vepoloxamer. Research-related manufacturing expenses include costs associated with producing and/or purchasing active pharmaceutical ingredient (API), conducting process development activities, producing clinical trial material, producing material for stability testing to support regulatory filings, related labeling, testing and release, packaging and storing services, related consulting fees, and costs related to purchasing nebulizers for administration of AIR001. Impairment losses on R&D-related manufacturing equipment are also considered research-related manufacturing expenses. Personnel costs relate to employee salaries, benefits and related costs.

A general understanding of drug development is critical to understanding our results of operations and, particularly, our R&D expenses. Drug development in the United States and most countries throughout the world is a process that includes several steps defined by the U.S. Food and Drug Administration, or FDA, and similar regulatory authorities in foreign countries. The FDA approval processes relating to new drug products differ depending on the nature of the particular product candidate for which approval is sought. With respect to any product candidate with active ingredients not previously approved by the FDA, a prospective drug product manufacturer is required to submit a NDA that includes complete reports of pre-clinical, clinical and laboratory studies and extensive manufacturing information to demonstrate the product candidate's safety and effectiveness. Generally, an NDA must be supported by at least phase 1, 2 and 3 clinical studies, with each study typically more expensive and lengthy than the previous study.

Future expenditures on R&D programs are subject to many uncertainties, including the number of clinical studies required to be conducted for each development program and whether we will develop a product candidate with a partner or independently. At this time, due to such uncertainties and the risks inherent in drug product development and the associated regulatory process, we cannot estimate with any reasonable certainty the duration of or costs to complete our R&D programs, or whether or when or to what extent revenues will be generated from the commercialization and sale of any of our product candidates. The duration and costs of our R&D programs, in particular, the duration and costs associated with clinical studies and research-related manufacturing, can vary significantly as a result of a variety of factors, including:

- the number of clinical and nonclinical studies necessary to demonstrate the safety and efficacy of a product candidate in a particular indication;
- the number of patients who participate in each clinical study;
- the number and location of sites included and the rate of site approval in each clinical study;
- the rate of patient enrollment and ratio of randomized to evaluable patients in each clinical study;
- the duration of patient treatment and follow-up;
- the potential additional safety monitoring or other studies requested by regulatory agencies;
- the time and cost to manufacture clinical trial material and commercial product, including process development and scale-up activities, and to conduct stability studies, which can last several years;

- the availability and cost of comparative agents used in clinical studies;
- the timing and terms of any collaborative or other strategic arrangements that we may establish; and
- the cost, requirements, timing of and the ability to secure regulatory approvals.

We regularly evaluate the prospects of our R&D programs, including in response to available scientific, nonclinical and clinical data, our assessments of a product candidate's market potential and our available resources, and make determinations as to which programs to pursue and how much funding to direct to each one.

As a result of cost-saving measures we have begun implementing, even if results from the EPIC study are positive, we expect our annual R&D expenses (excluding share-based compensation expense) will be approximately 5% to 10% less in 2016 compared to 2015. This decrease would be due primarily to less investment than previously anticipated in external costs related to preparing our vepoloxamer NDA, conducting our Phase 2 clinical study of vepoloxamer in heart failure, and research-related manufacturing for vepoloxamer.

Selling, General and Administrative Expenses. Selling, general and administrative, or SG&A, expenses consist primarily of salaries, benefits and related costs for personnel in executive, finance and accounting, legal and marketing functions, and professional and consulting fees for accounting, legal, investor relations, business development, commercial strategy and research, human resources and information technology services. Other SG&A expenses include facility lease and insurance costs and in-licensing costs for third-party intellectual property, if any.

As a result of cost-saving measures we have begun implementing, even if results from the EPIC study are positive, we expect our annual SG&A expenses (excluding share-based compensation expense) to be flat or approximately 5% less in 2016 compared to 2015. This decrease would be due primarily to less investment than previously anticipated in external costs related to commercial-readiness activities for vepoloxamer in sickle cell disease.

Interest Income. Interest income includes interest earned on our cash, cash equivalent and investment security balances.

Interest Expense. Interest expense consists of interest payments made and interest expense related to debt issuance costs and debt discount under our debt facility and interest expense associated with payments under capital leases of equipment.

Other (Expense)/Income, Net. Other (expense)/income, net includes unrealized and realized gains and losses from foreign currency transactions and other non-operating gains and losses.

Comparison of Three Months Ended June 30, 2016 and 2015

Revenue. We recognized no revenue for the three months ended June 30, 2016 and 2015.

R&D Expenses. Our most significant R&D expenses for the three months ended June 30, 2016 were external costs associated with the EPIC study, preparing our vepoloxamer NDA, research-related manufacturing for vepoloxamer and our Phase 2 study of vepoloxamer in heart failure. These expenses consisted primarily of CRO and CMO expenses, clinical study and regulatory-related consulting expenses, and study site expenses, which include start-up costs as well as patient costs. The following table summarizes our consolidated R&D expenses by type for each of the periods listed and their respective percent of our total R&D expenses for such periods (in thousands, except for percentages):

	Three Months Ended June 30,			
	2016	%	2015	%
External clinical study fees and expenses	$ 4,176	54%	$ 3,703	48%
External nonclinical study fees and expenses	2,338	30%	2,877	37%
Personnel costs	1,016	13%	1,013	13%
Share-based compensation expense	222	3%	141	2%
Total	$ 7,752	100%	$ 7,734	100%

R&D expenses were $7.8 million for the three months ended June 30, 2016 compared to $7.7 million the same period in 2015. Increases of $0.5 million in external clinical study fees and expenses and $0.1 million in share-based compensation expense were offset by a $0.5 million decrease in external nonclinical study fees and expenses during the 2016 period.

The $0.5 million increase in external clinical study fees and expenses was due primarily to increases of $0.7 million in costs for our Phase 2 study of vepoloxamer in heart failure and $0.4 million in costs for the Phase 2 studies of AIR001 in HFpEF, offset by decreases of $0.4 million in costs for the EPIC study and $0.2 million in costs for the Phase 2 study of vepoloxamer in acute limb

ischemia, or ALI, which we discontinued and began to wind-down in the third quarter of 2015. The $0.5 million decrease in external nonclinical study fees and expenses was due primarily to decreases of $1.2 million in research-related manufacturing costs and $0.4 million in costs for nonclinical studies of vepoloxamer, offset by increases of $0.9 million in external costs related to preparing our vepoloxamer NDA and $0.2 million in research-related manufacturing costs for AIR001.

SG&A Expenses. SG&A expenses were $2.4 million for the three months ended June 30, 2016, as well as for the same period in 2015.

Interest Expense. Interest expense for the three months ended June 30, 2016 was $512,000, $511,000 of which was related to our debt facility. There was $1,000 of interest expense in the three months ended June 30, 2015.

Net Loss. Net loss was $10.7 million, or $0.05 per share, for the three months ended June 30, 2016, compared to net loss of $10.2 million, or $0.06 per share, for the same period in 2015.

Comparison of Six Months Ended June 30, 2016 and 2015

Revenue. We recognized no revenue for the six months ended June 30, 2016 and 2015.

R&D Expenses. Our most significant R&D expenses for the six months ended June 30, 2016 were external costs associated with the EPIC study, research-related manufacturing for vepoloxamer, preparing our vepoloxamer NDA and our Phase 2 study of vepoloxamer in heart failure. These expenses consisted primarily of CRO and CMO expenses, clinical study and regulatory-related consulting expenses, and study site expenses, which include start-up costs as well as patient costs. The following table summarizes our consolidated R&D expenses by type for each of the periods listed and their respective percent of our total R&D expenses for such periods (in thousands, except for percentages):

	Six Months Ended June 30,			
	2016	%	2015	%
External clinical study fees and expenses	$ 8,230	52%	$ 7,210	52%
External nonclinical study fees and expenses	4,797	31%	4,393	32%
Personnel costs	2,143	14%	1,907	14%
Share-based compensation expense	457	3%	266	2%
Total	$ 15,627	100%	$ 13,776	100%

R&D expenses increased by $1.8 million, or approximately 13.4%, to $15.6 million for the six months ended June 30, 2016, compared to $13.8 million for the same period in 2015. This increase was due primarily to increases of $1.0 million in external clinical study fees and expenses, $0.4 million in external nonclinical study fees and expenses, $0.2 million in personnel costs and $0.2 million share-based compensation expense during the 2016 period.

The $1.0 million increase in external clinical study fees and expenses was due primarily to an increase of $1.2 million in costs for our Phase 2 study of vepoloxamer in heart failure and an increase of $0.4 million in costs for the Phase 2 studies of AIR001 in HFpEF, offset by a decrease of $0.5 million in costs for the Phase 2 study of vepoloxamer in ALI. The $0.4 million increase in external nonclinical study fees and expenses was due primarily to an increase of $1.4 million in external costs related to preparing our vepoloxamer NDA and an increase of $0.2 million in research-related manufacturing costs for AIR001, offset by decreases of $0.8 million in research-related manufacturing costs and $0.3 million in costs for nonclinical studies of vepoloxamer.

SG&A Expenses. SG&A expenses decreased by $0.7 million, or approximately 11.9%, to $5.3 million for the six months ended June 30, 2016, compared to $6.0 million for the same period in 2015. SG&A expenses in the six months ended June 30, 2015 included $0.4 million of severance expenses and $0.3 million of share-based compensation expense resulting from the termination of employment of our former president and chief operating officer in February 2015 and the acceleration of stock option vesting pursuant to the terms of his option agreements.

Interest Expense. Interest expense for the six months ended June 30, 2016 was $1,031,000, $1,029,000 of which was related to our debt facility. There was $1,000 of interest expense in the six months ended June 30, 2015.

Net Loss. Net loss was $21.9 million, or $0.12 per share, for the six months ended June 30, 2016, compared to net loss of $19.8 million, or $0.12 per share, for the same period in 2015.

Liquidity and Capital Resources

We have a history of annual losses from operations and we anticipate that we will continue to incur losses for at least the next several years. For the six months ended June 30, 2016, we incurred a loss from operations of $21.0 million. Our cash, cash equivalents and investment securities were $35.1 million and our working capital was $10.5 million as of June 30, 2016.

We historically have funded our operations principally through proceeds from sales of our equity securities. In February 2016, we completed an underwritten public offering with gross proceeds of $8.0 million from the sale and issuance of 29,090,910 units, each consisting of one share of our common stock and one warrant to purchase one share of our common stock. Net proceeds, after deducting underwriting discounts and commissions and other estimated offering expenses, were approximately $7.3 million. The warrants have an exercise price of $0.42 per share, are exercisable any time on or after August 17, 2016, subject to certain beneficial ownership limitations, and will expire on February 16, 2021.

We may receive up to $11.7 million, $18.3 million, $0.1 million, $16.5 million and $12.2 million of additional net proceeds from the exercise of warrants issued in the underwritten public offerings we completed in November 2011, June 2013, November 2014 and February 2016. However, the timing of the exercise and extent to which any of these warrants are exercised before they expire are beyond our control and depend on a number of factors, including certain beneficial ownership limitations and the market price of our common stock. The exercise prices of these warrants are $1.10, $0.65, $0.01, $0.75 and $0.42 per share, respectively. In comparison, the closing sale price of our common stock on August 5, 2016 was $0.34 per share and we do not expect the holders of the warrants to exercise them unless and until our common stock trades at or above the exercise price of their warrants. In addition, if at the time of exercise there is not an effective registration statement available for the issuance of the shares subject to the warrants, they may be exercised on a "cashless" net issuance basis, in which case we would not receive any proceeds from the exercise of these warrants.

In February 2014, we entered into a sales agreement with Cowen and Company, LLC, or Cowen, to sell shares of our common stock, with aggregate gross sales proceeds of up to $30.0 million, from time to time, through an ATM equity offering program, under which Cowen acts as sales agent. We refer to that agreement as the 2014 Sales Agreement. In August 2015, we terminated the 2014 Sales Agreement upon entry into a new sales agreement with Cowen to sell shares of our common stock, with aggregate gross sales proceeds of up to $30.0 million, from time to time, through an ATM program. As of June 30, 2016, we had sold an aggregate of 42,015,010 shares at a weighted-average sales price of $0.58 per share under the ATM programs for aggregate gross proceeds of $24.2 million and $23.1 million in aggregate net proceeds, after deducting sales agent commission and discounts and our other offering costs. As of June 30, 2016, 40,495,430 of the 42,015,010 shares sold had been issued; the remaining 1,519,580 shares sold were issued on July 1, 2016.

We have borrowed $15.0 million under a debt facility and have received proceeds of approximately $14.8 million, net of fees. Our principal balance as of August 5, 2016 was $14.1 million. The debt facility is governed by a loan and security agreement, as amended, among our company, Hercules Technology III, L.P., and Hercules Capital, Inc. (formerly known as Hercules Technology Growth Capital, Inc.), together referred to as Hercules. Under the loan and security agreement, as amended, we are required to prepay $10 million of the principal balance and any accrued but unpaid fees and expenses (referred to as the Second Advance Prepayment) unless, on or before October 14, 2016, we demonstrate, to the reasonable satisfaction of Hercules, positive results in the EPIC study (referred to as the Second Advance Prepayment Condition). In the event that the Second Advance Prepayment Condition is not satisfied, the Second Advance Prepayment would be due on October 14, 2016; provided, however, that if we issue a public announcement of EPIC results that do not satisfy the Second Advance Prepayment Condition before October 14, 2016, we are required to make the Second Advance Prepayment promptly, but in any case, within three business days of the public announcement. Our first principal payment of approximately $430,000 was paid on July 1, 2016. We will continue to repay the principal balance in equal monthly installments of principal and interest payments on the first business day of each month through the scheduled maturity date of January 1, 2019. However, if we achieve the Second Advance Prepayment Condition and no event of default has occurred, further principal payments will be deferred until March 1, 2017 and the scheduled maturity date will be extended from January 1, 2019 to October 1, 2019.

See Note 8, "Debt Facility," of the Notes to the Condensed Consolidated Financial Statements in this report for additional information regarding our debt facility with Hercules. Our obligations under our agreement with Hercules are secured by substantially all of our assets other than our intellectual property, but including proceeds from the sale, licensing or other disposition of our intellectual property. Our intellectual property is subject to negative covenants, which, among other things, prohibit us from selling, transferring, assigning, mortgaging, pledging, leasing, granting a security interest in or otherwise encumbering our intellectual property, subject to limited exceptions. The agreement includes a number of other restrictive covenants that may limit our ability to raise capital through other debt or equity financing. The debt facility also includes events of default, the occurrence and continuation of which would provide Hercules with the right to exercise remedies against us and the collateral securing our indebtedness, which include declaring payment of all or any part of the debt, together with an end of term charge of $712,500 and a prepayment charge of 1%, 2% or 3% of the then outstanding principal balance, immediately due and payable. These events of default include, among other things, our failure to pay any amount due on the due date, our breach or default in the performance of any covenant under the debt facility, our insolvency, the attachment, seizure, or filing of a levy against our assets or a judgment entered against us in an amount greater than $250,000, the occurrence of any default under certain other indebtedness, and, subject to limited exceptions, the occurrence of an

event or circumstance that would reasonably be expected to have a material adverse effect on our business, operations, assets or financial condition, our ability to repay our indebtedness in accordance with the terms of the debt facility, or on the collateral securing our indebtedness.

For a discussion of our liquidity and capital resources outlook, see "Management Outlook" below.

Operating activities. Net cash used in operating activities was $19.0 million for the six months ended June 30, 2016 and consisted primarily of a net loss of $21.9 million adjusted for non-cash items, including share-based compensation expenses of $1.3 million and amortization of debt issuance costs and debt discount of $0.3 million, and a net increase of $1.2 million due to changes in assets and liabilities. Net cash used in operating activities was $15.9 million for the six months ended June 30, 2015 and consisted primarily of a net loss of $19.8 million adjusted for non-cash items, including share-based compensation expenses of $1.6 million and a net increase of $2.2 million due to changes in assets and liabilities.

Investing activities. Net cash provided by investing activities was $7.4 million for the six months ended June 30, 2016 compared to net cash used in investing activities of $0.7 million for the same period in 2015. Net cash provided by investing activities for the six months ended June 30, 2016 was primarily due to $7.4 million in proceeds from the maturity of certificates of deposit. Net cash used in investing activities for the six months ended June 30, 2015 was primarily due to $8.0 million used to purchase certificates of deposit, offset by $7.3 million in proceeds from the maturity of certificates of deposit.

Financing activities. Net cash provided by financing activities was $13.0 million for the six months ended June 30, 2016 compared to $2.0 million for the same period in 2015. Net cash provided by financing activities for the six months ended June 30, 2016 was primarily a result of net proceeds of $7.3 million from the sale of units consisting of shares of our common stock and warrants to purchase our common stock in February 2016 and net proceeds of $5.8 million from the sale of common stock under our ATM equity offering program. Net cash provided by financing activities for the six months ended June 30, 2015 was primarily a result of net proceeds of $2.1 million from the sale of common stock under our ATM program, offset by $0.1 million in payments under a capital lease agreement for our phone equipment.

Management Outlook

If results from the EPIC study are positive and we believe they will support an NDA submission for vepoloxamer in sickle cell disease, we expect our operating expenses for the remaining six months of 2016 will be approximately $14.0 to $15.0 million, excluding share-based compensation expense. We have lowered our estimated operating expenses for 2016 because, while we remain focused on EPIC study database lock, we have implemented cost-saving measures in other areas, primarily by slowing down our investment in development and commercial-readiness activities for vepoloxamer in sickle cell disease and heart failure. In the case of negative results from the EPIC study, we plan to implement additional cost-saving measures that would further reduce our operating expenses. However, based on our projected capital needs in either scenario, our current cash, cash equivalents and investment securities and working capital will not be sufficient to fund our operations for the next 12 months. We intend to raise additional capital this year through our ATM program, other equity or debt financings, and/or through collaborations, including licensing arrangements, to pursue our current business strategy and planned operations. If we have positive results from the EPIC study but we are unable to raise sufficient additional capital, we anticipate that we would further reduce the scope of our planned operations during the fourth quarter of this year, including by further delaying or discontinuing investment in development and commercial-readiness activities for vepoloxamer in sickle cell disease and heart failure. In the event of negative results in the EPIC study and/or prepayment to Hercules on or before October 14, 2016 of $10.0 million of the principal balance under our debt facility, we plan to immediately and more drastically reduce the scope of our planned operations. In either case, we expect that our cash, cash equivalents and investment securities as of June 30, 2016, would be sufficient to fund our operations, as reduced in scope, into the first quarter of 2017. Whether results in the EPIC study are positive or negative, adequate additional capital may not be available to us on acceptable terms, on a timely basis, or at all. These uncertainties raise substantial doubt about our ability to continue as a going concern.

Our estimate of operating expenses for the remaining six months of 2016 and of the period of time through which our current financial resources will be adequate to support our operations are forward-looking statements based on significant assumptions. We could utilize our financial resources sooner than we currently expect. Forward-looking statements involve a number of risks and uncertainties and actual results could differ materially if the assumptions on which we have based our forward-looking statements prove to be wrong. Factors that will affect our 2016 operating expenses and future capital requirements include, but are not limited to:

- the results from the EPIC study and the timing of those results;
- feedback from the FDA after we have results from EPIC regarding the content and process for submission of an NDA for vepoloxamer, including whether the FDA will require a second Phase 3 study or other clinical or nonclinical studies to demonstrate substantial evidence of effectiveness of vepoloxamer for the treatment of sickle cell crisis, such as greater statistical significance or magnitude of clinical relevance, or to provide additional safety and tolerability data, or whether the FDA will require the starting material for vepoloxamer to be manufactured

consistent with cGMP requirements applicable to API or that we have control over excipient-grade cGMP conditions under which it currently is manufactured;

- our ability to secure adequate supply of API and finished drug product from our CMOs to meet market demand and manage our costs related to commercial manufacture of our products, should any of our product candidates obtain regulatory approval;
- the design, initiation, scope, rate of progress, results and timing of our clinical and nonclinical studies of our product candidates;
- the successful completion of our development programs and our ability to manage costs associated with clinical and nonclinical development of our product candidates, including research-related manufacturing activities;
- our ability to obtain and maintain regulatory approvals of our product candidates, the scope of regulatory approval we pursue, and the extent to which we do so independently or through collaborations;
- the extent to which we increase our workforce, including in connection with establishing a commercial infrastructure to support independent commercialization of vepoloxamer in the U.S. and EU, if approved;
- our ability to obtain and maintain effective patent coverage or other market exclusivity protections for our products, if approved, and to operate our business without infringing upon the intellectual property rights of others;
- the extent of commercial success of any of our product candidates for which we receive regulatory approval; and
- the extent to which we seek to expand our product pipeline through acquisitions and execute on transactions intended to do so.

Vepoloxamer

We are focusing our resources primarily on development of vepoloxamer. We completed patient enrollment in the EPIC study earlier this year and expect to report top-line data in September 2016. If results are positive, we plan to request a meeting with the FDA to assist in determining the content and process for submission of an NDA for vepoloxamer. Allocation of key resources to EPIC database lock procedures for longer than initially anticipated has affected our ability to prepare an NDA for vepoloxamer and prepare for a pre-NDA meeting with the FDA on previously anticipated timelines. Currently, we cannot predict with any certainty the timing of an NDA submission, potential FDA approval, or commercial launch of vepoloxamer. We plan to provide an updated timeline estimate following the results of the EPIC study and our pre-NDA meeting with the FDA. We continue to conduct activities to assist in the preparation of the NDA and in commercial-readiness, but plan to significantly ramp up these activities if EPIC results are positive and we are able to raise sufficient additional capital.

To support our NDA submission, we are conducting other studies in parallel with EPIC: an open-label, multicenter EPIC extension study known as EPIC-E to expand our existing safety database regarding repeat exposure to vepoloxamer; a sub-study of patients who participated in EPIC at selected U.S. study sites to investigate the effect of vepoloxamer on tissue oxygenation during sickle cell crisis; and a clinical pharmacokinetics study of vepoloxamer in approximately 40 individuals with varying degrees of renal insufficiency. The special population study will further enhance the safety database for vepoloxamer and help guide dosage adjustments for renally impaired patients. We intend to continue enrolling these studies as we prepare our NDA submission for vepoloxamer in sickle cell disease.

Vepoloxamer also is in Phase 2 clinical development for the treatment of heart failure. Our ongoing randomized, double-blind, placebo-controlled, multicenter Phase 2 study in which we plan to enroll approximately 150 patients, is evaluating a new formulation of vepoloxamer for the treatment of patients with chronic heart failure. As of August 5, 2016, we had opened a total of 10 study sites in the U.S. and Australia. Pending positive data from the EPIC study and if we are able to raise sufficient additional capital, we plan to open additional study sites within and outside of the U.S. Although predicting the rate and timing of enrollment for any clinical study including this study is subject to a number of significant assumptions and completion of the study may differ materially, we expect to complete patient enrollment in the first quarter of 2018. However, if results of the EPIC study are negative or we are unable to raise sufficient additional capital this year, we will need to review our plans and timing expectations for this Phase 2 study.

We also are evaluating vepoloxamer's potential in stroke. Based on nonclinical study data we announced in 2015, as well as published data from third party studies of poloxamer 188, we believe, and several medical experts in the field have agreed, that sufficient data now exists to support clinical development of vepoloxamer in stroke. We continue to assess the opportunity and believe it is a Phase 2-ready program. We do not plan to commence clinical development in stroke prior to analysis of results from the EPIC study. However, we recently were awarded a Small Business Innovation Research (SBIR) grant from the National Institute of

Neurological Disorders and Stroke of the National Institutes of Health in support of a nonclinical study of vepoloxamer to evaluate the effect of a combination treatment with vepoloxamer and tissue plasminogen activator in experimental models of embolic stroke.

Further, we are conducting or plan to conduct a number of other *ex vivo*, nonclinical *in vivo* and *in vitro* studies of vepoloxamer to further understand its pharmacologic effects and support our intellectual property positions.

AIR001

AIR001 is in Phase 2 clinical development for the treatment of patients with HFpEF. Since acquiring the program in 2014, we have supported investigator-sponsored Phase 2a studies of AIR001 in patients with HFpEF, one of which is ongoing and another of which reported positive top-line results in February 2016, as discussed above. In addition, as discussed above, we are supporting the INDIE-HFpEF study, a multicenter, randomized, double-blind, placebo-controlled crossover Phase 2 study of AIR001 in approximately 100 patients with HFpEF being conducted by the Heart Failure Clinical Research Network. The first patient was dosed in July 2016. The study will provide important data on the potential efficacy of AIR001 for patients with HFpEF and may result in patentable discoveries that help us protect the market for AIR001 products, if approved.

In parallel with our independent development of vepoloxamer and AIR001, from time to time, we evaluate opportunities for strategic collaborations, including with respect to country-specific development and regulatory or commercial expertise that would enhance the value of our programs.

As discussed above, based on our projected capital needs, we do not believe our current cash, cash equivalents and investment securities as of June 30, 2016 will be sufficient to meet our currently planned operations for the next 12 months and for the foreseeable future we must rely on equity and/or debt financings or collaborations such as licensing agreements to raise additional capital as and when needed. These circumstances raise substantial doubt about our ability to continue as a going concern. We intend to raise additional capital this year through our ATM program, other equity or debt financings, and/or through collaborations, including licensing arrangements, to pursue our current business strategy and planned operations. Subject to limited exceptions, our loan and security agreement with Hercules prohibits us from incurring indebtedness without Hercules' prior written consent. As discussed above, we have begun implementing cost-saving measures by delaying certain development and commercial-readiness activities for our vepoloxamer programs in sickle cell disease and heart failure. If we have positive results from the EPIC study but are unable to raise sufficient additional capital, we anticipate that we would further reduce the scope of our planned operations during the fourth quarter of this year, including by further delaying or discontinuing investment in development and commercial-readiness activities for vepoloxamer in sickle cell disease and heart failure. In the event of negative results in the EPIC study and/or prepayment to Hercules on or before October 14, 2016 of $10.0 million of the principal balance under our debt facility, we plan to immediately and more drastically reduce the scope of our operations. In either case, we expect that our cash, cash equivalents and investment securities as of June 30, 2016, would be sufficient to fund our operations, as reduced in scope, into the first quarter of 2017. We expect that the implementation of cost-saving measures to our NDA preparation and commercial-readiness activities will result in an extended timeline to submitting an NDA for approval of vepoloxamer in sickle cell disease even if EPIC results are positive and, ultimately, launching vepoloxamer in the U.S., if approved. In addition, delaying investment in manufacturing-related activities could adversely affect our ability to meet future market demand should vepoloxamer receive FDA approval. We cannot predict the effect of the cost-saving measures we are taking, or may yet take in 2016, on our development and commercialization timelines for vepoloxamer until after results of the EPIC study are known.

We may utilize our current financial resources sooner than we currently expect if we incur unanticipated expenses or the assumptions on which we've based our forecasts and contingency plans prove to be wrong. If we are unable to raise sufficient additional capital as needed and we reduce the scope of our operations, we may also be compelled to repay all of our outstanding debt to Hercules and sell certain assets, including intellectual property assets, which would have a further material and adverse effect on our financial condition and ability to pursue our business strategy.

Recent Accounting Pronouncements

See Note 11, "Recent Accounting Pronouncements," of the Notes to the Condensed Consolidated Financial Statements (Unaudited) in this report for a discussion of recent accounting pronouncements and their effect, if any, on us.

Forward Looking Statements

This report, particularly in Part I, Item 2, "Management's Discussion and Analysis of Financial Condition and Results of Operations," includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including, but not limited to, statements we make regarding our business strategy, expectations and plans, our objectives for future operations and our future financial position. When used in this report, the words "believe," "may," "could," "would," "will," "estimate," "continue," "anticipate," "plan," "intend,"

"expect," "indicate" and similar expressions are intended to identify forward-looking statements. Examples of forward-looking statements include, but are not limited to, statements we make regarding activities, timing and costs related to developing and seeking regulatory approval for our product candidates, including the nature, cost, and timing of initiation, completion and announcement of results of clinical studies and nonclinical testing, the indications in which we plan to pursue development of our product candidates, our plans regarding commercialization of our product candidates, if approved, our plans regarding partnering or other collaborative arrangements and for raising additional capital to support our operations, and our belief that our cash, cash equivalents and investment securities would be sufficient to fund a reduced level of operations into the first quarter of 2017. The foregoing is not an exclusive list of all forward-looking statements we make.

We have based the forward-looking statements we make on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, short-term and long-term business operations and objectives, and financial needs. The forward-looking statements we make are subject to known and unknown risks and uncertainties that could cause our actual results, performance or achievements to be materially different from any result, performance or achievement expressed or implied by the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to the following:

- negative results in the EPIC study;
- an event of default under our loan and security agreement with Hercules requiring us to repay all principal balance and accumulated interest and certain additional charges immediately, or our failure to demonstrate positive results in the EPIC study on or before October 14, 2016, which could require us to prepay $10.0 million of the principal balance;
- our ability to obtain additional capital in 2016, and the amount of additional capital we are able to raise, if any;
- the feedback from the FDA after we have results from EPIC regarding the content and process for submission of an NDA for vepoloxamer as a treatment for sickle cell crisis, including whether the FDA will require a second Phase 3 study or other clinical or nonclinical studies to demonstrate substantial evidence of effectiveness of vepoloxamer for the treatment of sickle cell crisis, or to provide additional safety and tolerability data, or whether the FDA will allow starting material for vepoloxamer to be manufactured consistent with cGMP requirements applicable to API or that we have control over excipient-grade cGMP conditions under which it currently is manufactured;
- our ability, or that of a future partner, to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates;
- our ability to establish effective sales and marketing capabilities and to timely launch our vepoloxamer product if approved for treatment of sickle cell crisis;
- delays in the commencement or completion of clinical studies or manufacturing and regulatory activities necessary to obtain regulatory approval to commercialize our product candidates, including vepoloxamer;
- suspension or termination of a clinical study, including due to patient safety concerns or capital constraints;
- our ability to successfully execute clinical studies, including timely enrollment, and the ability of our product candidates to demonstrate acceptable safety and efficacy in clinical studies;
- our ability to secure adequate and timely supply of API and finished drug product from our CMOs for clinical studies of our product candidates or, if approved, to meet market demand;
- the satisfactory performance of third parties, including CROs, on whom we rely significantly to conduct or assist in the conduct of our nonclinical testing, clinical studies and other aspects of our development programs;
- the potential for us to delay, scale back, or discontinue development of a product candidate, partner it at inopportune times, or pursue less expensive but higher-risk and/or lower-return development paths if we are unable to raise sufficient additional capital as needed;
- the potential for the FDA, or another regulatory agency, to require additional nonclinical or clinical studies of vepoloxamer or AIR001 prior to our initiation of a Phase 2 clinical study in any new indication;
- the potential that, even if clinical studies of a product candidate in one indication are successful, clinical studies of the same product candidate in another indication may not be successful;
- the potential for unsuccessful nonclinical or clinical studies in one indication or jurisdiction, or by a future partner that may be outside of our control, to adversely affect opportunities for a product candidate in other indications or jurisdictions;
- the potential that we may enter into one or more collaborative arrangements, including partnering or licensing arrangements, for a product candidate, and the terms of any such arrangements;

- the extent to which we increase our workforce and our ability to attract and retain qualified personnel and manage growth;
- the extent of market acceptance of our product candidates, if we receive regulatory approval, and available alternative treatments;
- our ability to obtain and maintain effective patent coverage or other market exclusivity protections for our products and technologies without infringing the proprietary rights of others;
- claims against us for infringing the proprietary rights of third parties;
- healthcare reform measures and reimbursement policies that, if not favorable to our products, could hinder or prevent commercial success;
- undesirable side effects that our product candidates or products may cause;
- potential product liability exposure and, if successful claims are brought against us, liability for a product or product candidate;
- the extent to which we acquire new technologies and/or product candidates and our ability to integrate them successfully into our operations;
- our ability to maintain compliance with NYSE MKT continued listing standards and to maintain the listing of our common stock on the NYSE MKT equities market or another national securities exchange; and
- the other factors that are described in Item 1A (Risk Factors) of Part II of this report.

Except as required by law, we do not intend to update the forward-looking statements discussed in this report publicly 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. In light of these risks and uncertainties and our assumptions, actual results may differ materially and adversely from expectations indicated or implied by the forward-looking statements contained in this report and in any documents incorporated in this report. Accordingly, you are cautioned not to place undue reliance on such forward-looking statements.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

Pursuant to Item 305(c) of Regulation S-K, we are not required to provide disclosures under this item until after December 31, 2016.

Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to provide reasonable assurance that information required to be disclosed by us in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can only provide reasonable assurance of achieving the desired control objectives, and in reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we have evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of June 30, 2016. Based on that evaluation, our principal executive officer and principal financial officer have concluded that as of June 30, 2016 these disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rules 13a-15(d) and 15d-15(d) under the Exchange Act that occurred during the quarterly period covered by this report that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings

From time to time, we may become involved in various claims and legal proceedings. Regardless of outcome, litigation and other legal and administrative proceedings can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors. We are not currently a party to any material pending litigation or other material legal proceeding.

Item 1A. Risk Factors

Investment in our securities involves a high degree of risk and uncertainty. Our business, operating results, growth prospects and financial condition are subject to various risks, many of which are not exclusively within our control, that may cause actual performance to differ materially from historical or projected future performance. We urge investors to consider carefully the risks described below, together with all of the information in this report, our annual report on Form 10-K for the year ended December 31, 2015 filed with the SEC on March 14, 2016 and our other public filings, before making investment decisions regarding our securities. Each of these risk factors, as well as additional risks not presently known to us or that we currently deem immaterial, could adversely affect our business, operating results, growth prospects or financial condition, as well as the trading price of our common stock, in which case you may lose all or part of your investment.

The risk factors set forth below that are marked with an asterisk (*) contain material changes to the similarly titled risk factors included in our annual report on Form 10-K for the year ended December 31, 2015 and our quarterly report on Form 10-Q for the quarterly period ended March 31, 2016.

RISKS RELATED TO OUR BUSINESS

Risks Related to Our Capital Requirements, Finances and Operations

We completed patient enrollment in our Phase 3 clinical study of vepoloxamer in sickle cell crisis (EPIC) earlier this year and top-line results are forthcoming. If EPIC results are not positive, our business, financial condition and results of operations could be materially adversely affected and the price of our common stock could decline significantly.*

None of our product candidates has been approved for sale by any regulatory agency or is available for commercial sale. Since 2012, we have focused our resources primarily on the development of vepoloxamer and the success of our business currently is highly dependent on the success of our Phase 3 clinical study of vepoloxamer for treatment of vaso-occlusive crisis in patients with sickle cell disease and our ability to obtain regulatory approval to market vepoloxamer in the United States. However, results from the EPIC study may not be positive or, even if the study demonstrates statistical significance in the primary endpoint, regulatory authorities may determine it does not demonstrate sufficient magnitude of clinical relevance or provide adequate safety and tolerability data to provide the basis for submission of a new drug application. If results from the EPIC study do not provide substantial evidence of vepoloxamer's efficacy and safety for the treatment of vaso-occlusive crisis, we would expect the FDA to require another Phase 3 study before accepting a NDA for vepoloxamer. Even if the FDA does not require another Phase 3 study, it may require other additional clinical or nonclinical studies to provide sufficient evidence of vepoloxamer's safety and tolerability. If results from the EPIC study are not positive in the sense that we or other market participants determine they are unlikely to provide a sufficient basis for FDA review or approval of a vepoloxamer NDA, we expect the price of our common stock to decline significantly and you could lose all of your investment. In addition, if we do not achieve the Second Advance Prepayment Condition, we will be required to prepay to Hercules $10 million of the principal balance under our debt facility on or before October 14, 2016. Further, in the event EPIC results are not positive, we plan to implement severe cost saving measures that likely would significantly delay our ability to complete development of vepoloxamer in sickle cell disease and to progress development of vepoloxamer and AIR001 in heart failure, and we may be compelled to not only to reduce the scope of our operations but also to sell or license our assets, including intellectual property assets, at less than we believe they should be valued. If EPIC results are not viewed as positive by us and others, our business, financial condition and results of operations will be significantly adversely impacted.

In addition, the allocation of key resources to the EPIC database lock process for longer than initially anticipated has affected our ability to prepare an NDA for vepoloxamer on previously anticipated timelines. Delays in submission of an NDA and, accordingly, in the commercial launch of vepoloxamer, if approved, could significantly increase development costs for that program and delays to market could adversely impact vepoloxamer's commercial success.

We have incurred net losses since our inception, we expect our operating expenses to continue to exceed revenue for the foreseeable future, and we may never generate revenue sufficient to achieve profitability. In addition, we do not believe our cash, cash equivalents and investment securities as of June 30, 2016 will be sufficient to fund our operations for the next 12 months and

we may not be able to raise additional capital as and when needed, which uncertainties raise substantial doubt regarding our ability to continue as a going concern.*

We are a clinical-stage biopharmaceutical company and have not generated sustainable revenue from operations or been profitable since inception, and we may never achieve profitability. We have devoted our resources to acquiring and developing proprietary product candidates, but such product candidates cannot be marketed until the regulatory process is completed and governmental approvals have been obtained. For the year ended December 31, 2015 and the six months ended June 30, 2016, we incurred losses from operations of $39.4 million and $21.0 million, respectively, and our net cash used in operating activities was $32.9 million and $19.0 million, respectively. At June 30, 2016, we had an accumulated deficit of $296.9 million, our cash, cash equivalents and investment securities were $35.1 million, and our working capital was $10.5 million. We expect to continue to incur substantial operating losses for the next several years as we advance our product candidates through clinical studies and other development activities and seek approval from the FDA and regulatory authorities outside of the U.S. to commercialize them. Accordingly, there is no current source of revenue from operations, much less profits, to sustain our present activities. Further, no revenue from operations will likely be available until, and unless, one of our product candidates is approved by the FDA or another regulatory agency and successfully marketed, or we enter into an arrangement that provides for licensing revenue or other partnering-related funding, outcomes which we may not achieve. If we obtain FDA approval of vepoloxamer in sickle cell disease, we may incur significant sales, marketing, and external manufacturing expenses, as well as continued research and development expenses. In addition, if we do not achieve the Second Advance Prepayment Condition, we will be required to prepay to Hercules $10.0 million of the principal balance under our debt facility on or before October 14, 2016.

As more fully discussed in Note 1 to the condensed consolidated financial statements included in this report and Part I, Item 2 “Management’s Discussion and Analysis of Financial Condition and Results of Operations” of this report, based on our anticipated operating expenses and current limited capital resources, we plan to raise additional capital in 2016 through our ATM program, other equity or debt financings, and/or through collaborations, including licensing arrangements, to fund our operations. However, our anticipated operating expenses and net losses and the uncertainties surrounding our ability to raise additional capital as needed raise substantial doubt about our ability to continue as a going concern. The condensed consolidated financial statements included in this report have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. However, if we are not successful in raising sufficient additional capital as needed, we may be compelled to reduce the scope of our operations and planned capital expenditures and/or sell or license certain assets at inopportune times, which could have a material and adverse effect on our ability to pursue our business strategy and our future financial condition.

Our management plans to take actions to raise additional capital to fund cash requirements after results of the EPIC study are known. However, there is no assurance that we will be able to obtain additional capital on favorable terms, or at all, or to successfully reduce costs in such a way that would continue to allow us to operate our business. If we are compelled to reduce the scope of our operations because we are unable to raise adequate additional capital as needed, which may be the case even if EPIC results are positive, our cost-saving measures may delay our ability to seek approval for vepoloxamer in sickle cell disease and/or to commercialize vepoloxamer for sickle cell crisis, if approved, and could adversely affect our ability to meet future market demand, which could have a material negative impact on our future financial condition and results of operations.

We cannot predict the extent of our future operating losses and accumulated deficit, and we may never generate sufficient revenues to achieve or sustain profitability. To become and remain profitable, we must succeed in developing and obtaining required regulatory approvals and commercializing our product candidates. This will require us to succeed in a range of challenging activities, including all of the activities described in our annual report on Form 10-K for the year ended December 31, 2015, and many aspects of drug development are inherently unpredictable. We may never succeed in obtaining the FDA’s or another regulatory authority’s approval to market our product candidates or otherwise generate revenues sufficient to achieve profitability. If we do achieve profitability, we may not be able to sustain it.

The success of our business currently is dependent largely on the success of vepoloxamer and if regulatory approval is delayed or not granted or, if granted, but our product is not commercially successful, our business, financial condition and results of operations may be materially adversely affected and the price of our common stock may decline.

None of our product candidates has been approved for sale by any regulatory agency or is available for commercial sale. We are focusing our resources primarily on the development of vepoloxamer. Accordingly, the success of our business currently is highly dependent on our ability, or that of a future partner, to successfully develop, obtain regulatory approval for and then successfully commercialize vepoloxamer and our efforts, or those of a future partner, in this regard may prove unsuccessful. The regulatory approval and successful commercialization of vepoloxamer is subject to many risks, including the risks discussed in other risk factors below, and vepoloxamer may not receive marketing approval from the FDA or any regulatory agency. If the results or timing of our clinical or nonclinical studies, regulatory filings, the regulatory process, regulatory developments, commercialization, and other activities, actions or decisions related to vepoloxamer do not meet our expectations or those of securities market participants, the market price of our common stock could decline significantly. If the FDA determines that the EPIC study does not provide sufficient efficacy and safety data for marketing approval, vepoloxamer may require costly additional clinical development prior to approval for treatment of vaso-occlusive crisis in patients with sickle cell disease in the United States. Even if the EPIC study is successful and

additional studies are not required prior to approval in sickle cell disease, regulatory approval and commercialization of vepoloxamer may be delayed or denied for a variety of reasons, including difficulties and/or delays in manufacturing and related activities or commercial launch activities, including hiring sales and marketing personnel and creating commercial infrastructure. If any of our product candidates is approved by the FDA or any foreign regulatory agency, our ability to generate revenue will depend in substantial part on the extent to which that drug product is accepted by the medical community and reimbursed by third-party payors, as well as our ability to market and sell the product and ensure that our third-party manufacturers produce it in quantities sufficient to meet commercial demand, if any.

The terms of our debt facility place restrictions on our operating and financial flexibility, and failure to comply with covenants or to satisfy certain conditions of the agreement governing the debt facility may result in acceleration of our repayment obligations and foreclosure on our pledged assets, which could significantly harm our liquidity, financial condition, operating results, business and prospects and cause the price of our common stock to decline.*

As of August 5, 2016, we had an outstanding principal balance of $14.1 million under our debt facility with Hercules Capital, Inc. and Hercules Technology III, L.P. (collectively referred to as Hercules) that is secured by a lien covering substantially all of our assets, excluding intellectual property, but including proceeds from the sale, licensing or disposition of our intellectual property. The loan and security agreement governing the debt facility requires us to comply with a number of covenants (affirmative and negative), including restrictive covenants that limit our ability to: incur additional indebtedness; encumber the collateral securing the loan; acquire, own or make investments; repurchase or redeem any class of stock or other equity interest; declare or pay any cash dividend or make a cash distribution on any class of stock or other equity interest; transfer a material portion of our assets; acquire other businesses; and merge or consolidate with or into any other organization or otherwise suffer a change in control, in each case subject to exceptions. Our intellectual property also is subject to customary negative covenants. In addition, subject to limited exceptions, Hercules could declare an event of default upon the occurrence of any event that it interprets as having a material adverse effect upon our business, operations, properties, assets, or financial condition or upon our ability to perform or pay the secured obligations under the loan and security agreement or upon the collateral or Hercules' liens on the collateral under the agreement, thereby requiring us to repay the loan immediately, together with a prepayment charge of up to 3% of the then outstanding principal balance and end-of-term charge of $712,500, or renegotiate the terms of the agreement. Although, in and of itself, the occurrence of adverse results or delays in any clinical study or the denial, delay or limitation of approval of or taking of any other regulatory action by the FDA or another governmental entity will not constitute a material adverse effect under our loan and security agreement with Hercules, Hercules may determine that such an event together with contemporaneous events or circumstances constitutes a material adverse effect upon our business, operations, properties, assets, or financial condition or upon our ability to perform or pay the secured obligations under the loan and security agreement. If we default under the facility, Hercules may accelerate all of our repayment obligations and, if we are unable to access funds to meet those obligations or to renegotiate our agreement, Hercules could take control of our pledged assets and we could immediately cease operations. If we were to renegotiate our agreement under such circumstances, the terms may be significantly less favorable to us. If we were liquidated, Hercules' right to repayment would be senior to the rights of our stockholders to receive any proceeds from the liquidation. Any declaration by Hercules of an event of default could significantly harm our liquidity, financial condition, operating results, business, and prospects and cause the price of our common stock to decline.

In addition, our loan and security agreement with Hercules, as amended to date, requires us to prepay $10 million of the principal balance on or before October 14, 2016, unless we have achieved the Second Advance Prepayment Condition. The $10 million prepayment to Hercules that could be required on or before October 14, 2016 may not only significantly harm our liquidity, financial condition and operating results and cause the price of our common stock to decline, but also significantly impair our ability to raise adequate additional capital to fund our operations and pursue our business strategy.

We will need to obtain additional funding to pursue our current business strategy and continue as a going concern and we may not be able to obtain such funding on a timely basis, or on commercially reasonable terms, or at all. Any capital-raising transaction we are able to complete may result in substantial dilution to our existing stockholders, require us to relinquish significant rights, or restrict our operations.*

As discussed above, based on our projected operating expenses and capital needs, our cash, cash equivalents and investment securities as of June 30, 2016, we intend to raise additional capital in 2016 through utilization of our ATM program, other equity or debt financings, and/or through collaborations, including licensing arrangements. If we are unable to raise sufficient additional capital as needed, or in the event of negative results in the EPIC study and prepayment to Hercules on or before October 14, 2016 of $10 million of the principal balance under our debt facility, we intend to significantly reduce the scope of our planned operations in the fourth quarter of 2016. In that case, we expect that our current cash, cash equivalents and investment securities will be sufficient to fund our operations, as reduced in scope, into the first quarter of 2017. The cost-saving measures we would implement in the event of results from EPIC are positive but we are unable to raise additional capital or in the event results from EPIC are negative, likely would further delay our ability to complete development of vepoloxamer in sickle cell disease, obtain regulatory approval to commercialize vepoloxamer, and, if approved, may adversely affect our ability to meet market demand, as well as impair progress on our other development programs. In addition, we may utilize our current financial resources sooner than we currently expect if we incur unanticipated expenses or the assumptions on which we have based our forecasts and contingency plans prove to be wrong.

Although we were able to raise significant funds in the past through equity financings and a debt financing, the conditions of and our access to capital markets are highly variable and adequate additional equity or debt financing may not be available to us in the future on acceptable terms, or on a timely basis, or at all. Further, each of these financing alternatives carries risks. Raising capital through the issuance of our common stock, or securities convertible into or exercisable for our common stock, may depress the market price of our stock and may substantially dilute our existing stockholders. If instead we seek to raise capital through strategic transactions, such as licensing arrangements or sales of one or more of our technologies or product candidates, we may be required to relinquish valuable rights and dilute the current and future value of our assets. For example, any licensing arrangement likely would require us to share with our licensee a significant portion of any revenues generated by our licensed technologies. Additionally, our control over the development and/or marketing of any products or product candidates licensed or sold to third parties likely would be reduced and thus we may not realize the full value of any such products or product candidates. Debt financings would likely involve covenants and/or repayment provisions that would restrict our operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of our assets, including requirements to maintain specified amounts of cash or restrictions on our ability to license or sell our intellectual property assets, as well as prohibitions on our ability to create liens or make investments and may, among other things, preclude us from making distributions to stockholders (either by paying dividends or redeeming stock) and taking other actions beneficial to our stockholders. In addition, investors could impose more one-sided investment terms and conditions on companies that have or are perceived to have limited remaining funds or limited ability to raise additional funds. The lower our cash balance, the more difficult it is likely to be for us to raise additional capital on commercially reasonable terms, or at all.

For particular development programs, such as development of vepoloxamer for resuscitation following major trauma, we plan to seek funding from the U.S. government. The process of obtaining government contracts is lengthy and uncertain and highly competitive. In addition, changes in government budgets and agendas may result in decreased availability of funding for drug research and development. If we do secure government funding, the contracts for such funding may contain termination and audit provisions that are unfavorable to us and cause us to incur significant additional administrative expense. In addition, the U.S. government may require "march-in" rights that allow it to grant licenses to inventions that arise from development programs it funds if, for example, we do not commercialize the technology within a certain timeframe or the government deems such action necessary to alleviate health or safety needs that are not being reasonably satisfied by us. If the government exercises its march-in rights, we could be obligated to license intellectual property developed by us on terms unfavorable to us and we may not receive compensation from the government for its exercise of such rights.

Notwithstanding efforts on our part to raise additional capital, adequate additional funding may not be available on acceptable terms, or on a timely basis, or at all. Even if we incur costs in pursuing, evaluating and negotiating particular capital-raising and/or strategic or partnering transactions, our efforts may not prove successful. We believe global economic conditions, such as volatility in the U.S. and international equity markets, may adversely impact our ability to raise additional capital. Our failure to raise capital as needed would have a material adverse effect on our financial condition and ability to pursue our business strategy and we potentially may be unable to continue as a going concern and required to liquidate our assets and dissolve our company.

If we are unable to raise sufficient additional capital as needed, we may be forced to delay, reduce or discontinue development of our product candidates and commercialization efforts, partner them or dispose of our assets at inopportune times or pursue less expensive but higher-risk and/or lower-return development paths.

If we are not able to raise sufficient additional capital as needed, we may be required to delay, reduce or discontinue one or more of our development programs and commercialization efforts, to seek collaborators or buyers at an earlier stage than otherwise would be desirable or on terms less favorable than might otherwise be available, or to liquidate our assets and dissolve our company. For example, if we do not have sufficient capital, we may determine to delay or suspend planned or ongoing clinical or nonclinical studies or other development activities and/or not to investigate certain additional indications for vepoloxamer or to conduct other studies or activities intended to enhance our intellectual property position, improve the probability of regulatory approval, or expand the scope of vepoloxamer's clinical benefit and market potential, or we may not make investments desirable for commercial success of vepoloxamer as a treatment for sickle cell crisis, if approved. Delays in and/or reduction of development and commercial-readiness activities could impair our ability to realize the full clinical and market potential of a product candidate and have a material adverse effect on our business and financial condition. In addition, suspension or discontinuation of a development program may be viewed negatively, which could adversely affect our stock price.

To the extent we discontinue independent development of a product candidate, we may not realize any value from our investment in the discontinued program. Even if we pursue a strategic option, such as partnering, selling or exclusively licensing the program to a third party, such an option may not be available on acceptable terms or at all. For example, in prior years, we were focused on developing Exelbine and ANX-514 and expended significant resources on their development; however, in 2011 and 2012, respectively, we elected to discontinue independent development of those programs. Although from time to time we evaluate other opportunities for further development of those agents, such as partnering and licensing arrangements, none may be available and we may not realize any return on our investment in those programs.

In addition, if we determine our financial resources are insufficient to fund our operations even after implementing significant cost saving measures and reducing the scope of our operations, we may be required to dispose of or liquidate our assets at values significantly less than what we believe their values to be and at which they are carried on our financial statements.

The process of developing and seeking regulatory approval of, and ultimately commercializing, investigational new drug products requires expenditure of substantial resources, and we cannot estimate with reasonable certainty the duration of or costs to complete our development programs.

Our capital requirements for the foreseeable future will depend in large part on, and could increase significantly as a result of, our expenditures on our development programs. Future expenditures on our development programs are subject to many uncertainties, and will depend on, and could increase significantly as a result of, many factors, including:

- the number, size, complexity, results and timing of our drug development programs;
- the number of clinical and nonclinical studies necessary to demonstrate acceptable evidence of the safety and efficacy of a product candidate in a particular indication;
- the number of patients who participate, the rate of enrollment, and the ratio of randomized to evaluable patients in each clinical study;
- the number and location of sites and the rate of site initiation in each study;
- the duration of patient treatment and follow-up;
- the potential for additional safety monitoring or other post-marketing studies that may be requested by regulatory agencies;
- the time and cost to manufacture clinical trial material and commercial product, including process development and scale-up activities, and to conduct stability studies, which can last several years;
- the degree of difficulty and cost involved in securing alternate manufacturers or suppliers of drug product, components or delivery devices, as necessary to meet FDA requirements and/or commercial demand;
- the costs, requirements, timing of, and the ability to, secure regulatory approvals;
- the timing and terms of any collaborative or other strategic arrangement that we may establish;
- the extent to which we increase our workforce and the costs involved in recruiting, training and incentivizing new employees;
- the costs related to developing, acquiring and/or contracting for sales, marketing and distribution capabilities, supply chain management capabilities, and regulatory compliance capabilities, if we obtain regulatory approval for a product candidate and commercialize it without a partner;
- competing technologies and market developments; and
- the costs involved in establishing, enforcing or defending patent claims and other proprietary rights.

We may not be able to raise capital when needed or reduce other expenditures to offset expenditures on our development programs, which could have a material adverse effect on our financial condition and ability to pursue our business strategy.

Our ability to raise capital may be limited by applicable laws and regulations.

Historically, we have raised capital primarily through the sale of our equity securities. In recent years, we have raised substantial funding through equity offerings conducted under "shelf" registration statements on Form S-3. Using a shelf registration statement on Form S-3 to raise additional capital generally takes less time and is less expensive than other means, such as conducting an offering under a Form S-1 registration statement. However, our ability to raise capital using a shelf registration statement may be limited by, among other things, current SEC rules and regulations. Under current SEC rules and regulations, we must meet certain requirements to use a Form S-3 registration statement to raise capital without restriction as to the amount of the market value of securities sold thereunder. One such requirement is that the market value of our outstanding common stock held by non-affiliates, or public float, be at least $75.0 million as of a date within 60 days prior to the date of filing the Form S-3. If we do not meet that requirement, then the aggregate market value of securities sold by us or on our behalf under the Form S-3 in any 12-month period is limited to an aggregate of one-third of our public float. Moreover, even if we meet the public float requirement at the time we file a Form S-3, SEC rules and

regulations require that we periodically re-evaluate the value of our public float, and if, at a re-evaluation date, our public float is less than $75.0 million, we would become subject to the one-third of public float limitation described above. If our ability to utilize a Form S-3 registration statement for a primary offering of our securities is limited to one-third of our public float, we may conduct such an offering pursuant to an exemption from registration under the Securities Act or under a Form S-1 registration statement, which we have done in the past, including in June 2013, and we would expect either of those alternatives to increase the cost of raising additional capital relative to utilizing a Form S-3 registration statement.

In addition, under current SEC rules and regulations, our common stock must be listed and registered on a national securities exchange in order to utilize a Form S-3 registration statement (i) for a primary offering, if our public float is not at least $75.0 million as of a date within 60 days prior to the date of filing the Form S-3, or a re-evaluation date, whichever is later, and (ii) to register the resale of our securities by persons other than us (i.e., a resale offering). While currently our common stock is listed on the NYSE MKT equities market, there can be no assurance that we will be able to maintain such listing. The NYSE MKT reviews the appropriateness of continued listing of any issuer that falls below the exchange's continued listing standards. Previously, including during part of 2010, we were not in compliance with certain NYSE MKT continued listing standards and were at risk of having our common stock delisted from the NYSE MKT equities market. For additional information regarding this risk, see the risk factor below titled "If we are unable to maintain compliance with NYSE MKT continued listing standards, our common stock may be delisted from the NYSE MKT equities market, which would likely cause the liquidity and market price of our common stock to decline."

Our ability to timely raise sufficient additional capital also may be limited by the NYSE MKT's stockholder approval requirements for transactions involving the issuance of our common stock or securities convertible into our common stock. For instance, the NYSE MKT requires that we obtain stockholder approval of any transaction involving the sale, issuance or potential issuance by us of our common stock (or securities convertible into our common stock) at a price less than the greater of book or market value, which (together with sales by our officers, directors and principal stockholders) equals 20% or more of our then outstanding common stock, unless the transaction is considered a "public offering" by the NYSE MKT staff. Based on 211,815,450 shares of our common stock outstanding as of August 5, 2016 and the closing price per share of our common stock on such date, which was $0.34, we could not raise more than approximately $14.4 million without obtaining stockholder approval, unless the transaction is deemed a public offering or does not involve the sale, issuance or potential issuance by us of our common stock (or securities convertible into our common stock) at a price less than the greater of book or market value. In addition, certain prior sales by us may be aggregated with any offering we may propose in the future, further limiting the amount we could raise in any future offering that is not considered a public offering by the NYSE MKT staff and involves the sale, issuance or potential issuance by us of our common stock (or securities convertible into our common stock) at a price less than the greater of book or market value. The NYSE MKT also requires that we obtain stockholder approval if the issuance or potential issuance of additional shares will be considered by the NYSE MKT staff to result in a change of control of our company.

Obtaining stockholder approval is a costly and time-consuming process. If we are required to obtain stockholder approval for a potential transaction, we would expect to spend substantial additional money and resources. In addition, seeking stockholder approval would delay our receipt of otherwise available capital, which may materially and adversely affect our ability to execute our current business strategy, and there is no guarantee our stockholders ultimately would approve a proposed transaction. A public offering under the NYSE MKT rules typically involves broadly announcing the proposed transaction, which often times has the effect of depressing the issuer's stock price, as occurred following our issuance of a press release on February 9, 2016 announcing a proposed underwritten public offering. Accordingly, the price at which we could sell our securities in a public offering may be less, and the dilution existing stockholders experience may in turn be greater, than if we were able to raise capital through other means.

We have significant goodwill and IPR&D and impairment of goodwill and IPR&D may have a significant adverse impact on our future financial condition and results of operations.

Our goodwill and IPR&D assets, which resulted from our acquisitions of SynthRx and Aires Pharmaceuticals in 2011 and 2014, respectively, represent a significant portion of our total assets. As of June 30, 2016, we had goodwill and IPR&D of approximately $11.6 million, representing approximately 24% of our total assets. These intangible assets are subject to an impairment analysis whenever an event or change in circumstances indicates the carrying amount of such an asset may not be recoverable. We test our goodwill and IPR&D for impairment annually, or more frequently if an event or change in circumstances indicates that the asset may be impaired. If an impairment exists, we would be required to record an impairment charge with respect to the impaired asset to our consolidated statements of operations and comprehensive loss. A significant impairment charge could have a material negative impact on our financial condition and results of operations.

Events giving rise to impairment are difficult to predict and are an inherent risk in the pharmaceutical industry. Some of the potential risks that could result in impairment of our goodwill and IPR&D include negative clinical study results, adverse regulatory developments, delay or failure to obtain regulatory approval, additional development costs, changes in the manner of our use or development of vepoloxamer or AIR001, competition, earlier than expected loss of exclusivity, pricing pressures, higher operating costs, changes in tax laws, and other market and economic environment changes or trends. All of our goodwill and approximately $6.5 million of our IPR&D, or approximately 83% of our total goodwill and IPR&D, relate to the fair value of our vepoloxamer program in sickle cell disease as of the date we acquired SynthRx. If, for example, results from the EPIC study are negative or, based

on pre-NDA discussions with the FDA, we determine that additional development costs will be necessary to obtain regulatory approval, we may re-evaluate our goodwill and IPR&D and be required to incur a significant non-cash impairment charge, which could materially adversely affect our financial condition and results of operations.

Our business may suffer if we are unable to retain and attract highly qualified personnel and manage internal growth.

Currently, we have a small number of employees and we rely on third parties to perform many essential services for us. Our ability to execute on our business strategy and compete in the highly competitive biopharmaceutical, specialty pharmaceutical, pharmaceutical and biotechnology industries depends, in part, on our ability to attract and retain highly qualified personnel. Our industries in general and our company in particular historically have experienced a high rate of turnover of management personnel. Loss of key employees, including any of our executive officers, could adversely affect our ability to successfully execute our current business strategy, which could negatively affect our stock price. Replacing key employees may be a difficult, costly and protracted process, particularly due to the fact that we may not have other personnel with the capacity to assume all of the responsibilities of a key employee. In addition, we may seek to increase the size of our organization as development of our product candidates progresses, and in particular, in connection with independent commercialization of vepoloxamer as a therapy for patients with sickle cell disease, if approved by the FDA. There is intense competition from other companies and organizations for qualified personnel in the areas of our activities. Other companies and organizations with which we compete for personnel may have greater financial and other resources and different risk profiles than we do, and a history of successful development and commercialization of their product candidates, which may make them more attractive employers. Our ability to compete for qualified personnel also may be adversely affected by our highly volatile stock price. The value of stock options we offer to candidates to induce their employment and to our employees to retain and incentivize them is significantly affected by movements in our stock price that we cannot control and may at any time be insufficient to counteract more lucrative offers from other companies. All of our employees, including our executive officers, may terminate their employment with us at any time without notice. If we cannot attract and retain skilled personnel, as needed, we may not achieve our development and other goals.

Future internal growth could impose significant added responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees. We may need to devote a significant amount of time to managing these activities and may not be able to do so effectively. If we are unable to effectively manage future internal growth, our expenses may increase more than expected, we may not be able to achieve our development goals, and our ability to generate and/or grow revenue could be diminished. In the meantime, the success of our business also depends, in part, on our ability to develop and maintain relationships with respected service providers and industry-leading consultants and advisers. If we cannot develop and maintain such relationships, as needed, the rate and success at which we can develop and commercialize product candidates may be limited. In addition, our outsourcing strategy, which has included engaging consultants that spend considerable time in our office to manage key functional areas, may subject us to scrutiny under labor laws and regulations, which may divert management time and attention and have an adverse effect on our business and financial condition.

If we determine to grow our business through the acquisition of new technologies and/or product candidates, our existing stockholders may experience substantial dilution, we may fail to realize the benefits of any future strategic acquisition or investment, and we may incur unexpected costs and disruptions to our business.

From time to time, we may evaluate pipeline expansion opportunities and execute the acquisition of new technologies and/or product candidates that we believe will increase the long-term value of our company. The process of identifying, evaluating, negotiating and implementing the purchase or license of new assets is lengthy and complex and may be disruptive to our operations and/or distracting for our personnel. We have limited resources with respect to identifying, evaluating, negotiating and implementing the acquisition of new assets or rights thereto and integrating them into our current infrastructure. Supplementing our current resources to complete one or more of these transactions may be costly.

We may use cash, shares of our common stock, securities convertible into or exercisable for shares of our common stock or a combination of cash and our securities to pay the purchase price or license fee for any future strategic transaction. The use of cash could negatively impact our financial position and ability to advance our current development programs. The use of shares of our common stock or securities convertible into or exercisable for shares of our common stock would dilute the holdings of our existing stockholders and such dilution could be substantial. For example, to acquire SynthRx we agreed to issue up to such number of shares that represented a 41% ownership stake in our company at the time we completed the acquisition in April 2011, if development of vepoloxamer fully achieved the milestones under the merger agreement. The issuance of shares in connection with future strategic transactions, if any, may result in the stockholders who own the majority of our voting securities prior to one or more of such transactions owning less than a majority after such transactions.

Further, strategic transactions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;

- disruption of our business and diversion of our management's time and attention to develop and/or commercialize acquired technologies and/or product candidates;
- incurrence of substantial debt to pay for acquisitions;
- greater than anticipated difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers of any acquired business due to changes in management and ownership; and
- inability to retain key employees of any acquired business.

Our stockholders will be required to rely on the judgment of our management and board of directors as to which new product candidates and/or technologies we pursue and may have limited or no opportunity to evaluate potential new assets prior to completion of a transaction, including the terms of acquisition, the costs of their future development and their commercial potential. We may devote resources to potential acquisition or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. Any technology and/or product candidate that we acquire or to which we acquire rights likely will require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are subject to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities and other risks described under the section titled "Risks Related to Drug Development and Commercialization."

We expend substantial resources to comply with laws and regulations relating to public companies, and any failure to maintain compliance could subject us to regulatory scrutiny and cause investors to lose confidence in our company, which could harm our business and have a material adverse effect on our stock price.

Laws and regulations affecting public companies, including provisions of the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 and the Sarbanes-Oxley Act of 2002, or SOX, and the related rules and regulations adopted by the SEC and by the NYSE MKT have resulted in, and will continue to result in, significant costs to us as we evaluate the implications of these rules and respond to their requirements. For example, compliance with Section 404 of SOX, including performing the system and process documentation and evaluation necessary to issue our annual report on the effectiveness of our internal control over financial reporting and, if applicable, obtain the required attestation report from our independent registered public accounting firm, requires us to incur substantial expense and expend significant management time. Further, we have in the past discovered, and may in the future discover, areas of internal controls that need improvement. If we identify deficiencies in our internal controls that are deemed to be material weaknesses, we could become subject to scrutiny by regulatory authorities and lose investor confidence in the accuracy and completeness of our financial reports, which could have a material adverse effect on our stock price. Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations, including the possibility of human error and circumvention by collusion or overriding of controls. Accordingly, even an effective internal control system may not prevent or detect material misstatements on a timely basis, or at all. Also, previously effective controls may become inadequate over time as a result of changes in our business or operating structure, and we may fail to take measures to evaluate the adequacy of and update these controls, as necessary, which could lead to a material misstatement.

In addition, new laws and regulations could make it more difficult or more costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the coverage that is the same or similar to our current coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees, and as our executive officers. We cannot predict or estimate with any reasonable accuracy the total amount or timing of the costs we may incur to comply with these laws and regulations.

Our ability to use net operating loss carry forwards and research and development tax credits to offset future taxable income or future tax will be limited, and may be limited further in the future, due to changes in ownership (within the meaning of IRC Section 382) that have occurred and may occur in the future.

In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or IRC, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, and certain other tax assets to offset future taxable income, and an ownership change is generally defined as a cumulative change of 50% or more in the ownership positions of certain stockholders during a rolling three-year period. In 2012, we had identified an ownership change within the meaning of IRC Section 382 that occurred on November 11, 2011 as a result of an equity financing we completed on that date and, consequently, we do not expect to be eligible to utilize the NOL carry forwards and research and development tax credits we had accumulated as of November 11, 2011. We completed a formal study to determine if any ownership changes within the meaning of IRC Section 382 had occurred during the years ended December 31, 2012, 2013 and 2014. None were identified. However, other

ownership changes within the meaning of IRC Section 382 may occur in the future or may already have occurred in connection with the public offering of our common stock and warrants completed in February 2016, which could eliminate or restrict our ability to use NOL carry forwards and research and development tax credits generated after November 11, 2011. Limitations on our ability to use NOL carry forwards and research and development tax credits to offset future taxable income could require us to pay U.S. federal income taxes earlier than would be required if such limitations were not in effect. Similar rules and limitations may apply for state income tax purposes.

Our business and operations would suffer in the event of computer system failures, cyber-attacks on our systems or deficiency in our cyber security.

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, malware, natural disasters, fire, terrorism, war and telecommunication, electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, our systems or those of third parties on which we rely safeguard important confidential personal data regarding our employees and patients enrolled in our clinical trials. If a disruption event were to occur and cause interruptions in our operations, it could result in a disruption of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of vepoloxamer, AIR001 and any future product candidates we may develop could be delayed.

Our employees, independent contractors and consultants, principal investigators, CROs, CMOs and other vendors, and any future commercial partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk that our employees, independent contractors and consultants, principal investigators, CROs, CMOs and other vendors, and any future commercial partners may engage in fraudulent conduct or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, to provide accurate information to the FDA or comparable foreign regulatory authorities, to comply with manufacturing standards required by cGMP or that we establish, to comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, and to report financial information or data accurately or disclose unauthorized activities to us. The misconduct of our employees and others we engage to provide services to us could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We maintain a code of business conduct and ethics for our directors, officers and employees, but it is not always possible to identify and deter such misconduct, 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 be in compliance with such laws or regulations. 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 and results of operations, including the imposition of significant fines or other sanctions.

Laws and regulations governing conduct of international operations may negatively impact our development, manufacture and sale of products outside of the United States and require us to develop and implement costly compliance programs.

Currently, except for our clinical study sites and manufacturing activities performed by third party vendors located outside of the United States, substantially all of our operations are in the U.S. However, we may seek to expand our operations outside of the U.S., particularly as we seek to commercialize our product candidates outside of the U.S., and we must comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The creation and implementation of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where we must rely on third parties.

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring such companies to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-

bribery provisions of the FCPA are enforced primarily by the U.S. Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the U.S., or the sharing with certain foreign nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Expanding our presence outside of the U.S. will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling our product candidates outside of the U.S., which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. Additionally, the SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

Our operations might be interrupted by the occurrence of a natural disaster or other catastrophic event.

Our corporate headquarters are located in a single commercial facility in San Diego, California. Important documents and records, including copies of our regulatory documents and other records for our product candidates, are located at our facilities and we depend on our facilities for the continued operation of our business. Natural disasters and other catastrophic events, such as wildfires and other fires, earthquakes and extended power interruptions, which have impacted San Diego businesses in the past, and terrorist attacks or severe weather conditions, could significantly disrupt our operations and result in additional, unplanned expense. As a small company with limited resources, we have not prepared or implemented a formal business continuity or disaster recovery plan and any natural disaster or catastrophic event could disrupt our business operations and result in setbacks to our development programs. Even though we believe we carry commercially reasonable insurance, we might suffer losses that are not covered by or exceed the coverage available under these insurance policies.

Risks Related to Drug Development and Commercialization

There is significant uncertainty regarding the regulatory approval process for any investigational new drug, including vepoloxamer, further testing and validation of our product candidates and related manufacturing processes are required, and regulatory approval may be conditioned, delayed or denied, which could delay or prevent us from successfully marketing our product candidates and substantially harm our business.

Human pharmaceutical products generally are subject to rigorous nonclinical testing and clinical studies and other approval procedures mandated by the FDA and foreign regulatory authorities. Various federal and foreign statutes and regulations also govern or influence the manufacturing, safety, labeling, storage, record keeping and marketing of pharmaceutical products. The process of obtaining these approvals and the subsequent compliance with appropriate U.S. and foreign statutes and regulations is time-consuming and requires the expenditure of substantial resources.

Significant uncertainty exists with respect to the regulatory approval process for any investigational new drug, including vepoloxamer for patients with sickle cell disease. Regardless of guidance the FDA may give a drug's sponsor during its development, the FDA retains complete discretion in deciding whether to accept a NDA for filing or, if accepted, approve an NDA. There will be many components to our NDA submission for vepoloxamer beyond the data from the EPIC and EPIC-E studies. For example, in addition to reviewing the safety and efficacy data from EPIC and EPIC-E and from clinical and nonclinical studies of poloxamer 188 and/or vepoloxamer completed, in some cases, more than 20 years ago, the FDA will review our internal systems and processes, as well as those of our CROs, CMOs and other vendors, related to development of our product candidate, including those pertaining to our clinical studies and manufacturing processes. Before accepting an NDA for vepoloxamer or before approving the NDA, the FDA may request that we provide additional information that may require significant resources and time to generate and there is no guarantee that our product candidate will be approved for the treatment of vaso-occlusive crisis in patients with sickle cell disease or any other indication. The FDA may choose not to approve our NDA for vepoloxamer for any of a variety of reasons, including a decision related to the safety or efficacy data, manufacturing controls or systems, or for any other issues that the agency may identify related to the development of our product candidate. Even if the EPIC study is successful in providing statistically significant evidence of the

efficacy and safety of vepoloxamer to treat vaso-occlusive crisis of sickle cell disease, the FDA may not consider efficacy and safety data from a single Phase 3 study adequate scientific support for a conclusion of effectiveness and/or safety and may require an additional Phase 3 or other studies prior to granting marketing approval. If this were to occur, the overall development cost for vepoloxamer in sickle cell disease would be substantially increased and an alternative therapy could be approved and introduced to the market in the meantime, which could adversely affect our business, financial condition and results of operations.

We expect our MAST platform to accelerate development of vepoloxamer as compared to other new molecular entities for therapeutic use in humans. However, this expectation is predicated on the belief that regulatory authorities, such as the FDA, will consider clinical and nonclinical studies of vepoloxamer and poloxamer 188 conducted by prior sponsors supportive of our clinical development of vepoloxamer, which may not be the case for a variety of reasons, including that an agency may not agree that the test material in prior-sponsor studies was the same as or similar enough to the test material in our studies. If regulatory agencies take the position that prior-sponsor studies of vepoloxamer and poloxamer 188 do not support the safety and efficacy of our vepoloxamer-based product candidates, they may require further testing of our product candidates prior to granting marketing approval, which could require us to expend substantial additional resources and significantly delay commercialization of our product candidates.

Further, development of our product candidates and/or regulatory approval may be delayed for reasons beyond our control. For example, U.S. federal government shut-down or budget sequestration, such as occurred during 2013, may result in significant reductions to the FDA's budget and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of or obtain regulatory approval for our product candidates.

Even if the FDA grants approval, the conditions or scope of the approval may limit our ability to commercialize our product, and in turn, limit our ability to generate substantial sales revenue. For example, the FDA may not approve the labeling claims for our vepoloxamer product that we believe are necessary or desirable for successful commercialization as a treatment for sickle cell disease, or may grant approval contingent on the performance of costly post-approval clinical trials or subject to warnings or contraindications. Additionally, even after granting approval, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for our product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, and continued compliance with current good manufacturing processes, or cGMP, good clinical practices, international conference on harmonization regulations and good laboratory practices, which are regulations and guidelines that are enforced by the FDA for all of our clinical development and for any clinical studies that we conduct post-approval. The FDA may decide to withdraw approval, add warnings or narrow the approved indications in the product label, or establish risk management programs that could restrict distribution of our products. These actions could result from, among other things, safety concerns, including unexpected side effects or drug-drug interaction problems, or concerns over misuse of a product. If any of these actions were to occur following approval, we may have to discontinue commercialization of the product, limit our sales and marketing efforts, and/or conduct post-approval studies, which in turn could result in significant expense and delay or limit our ability to generate sales revenues.

Clinical studies typically involve a lengthy and expensive process with an uncertain outcome.

Clinical testing typically is expensive and can take years to complete, and its outcome is inherently uncertain. Clinical studies may not commence on time or be completed on schedule, if at all. The commencement and completion of clinical studies can be delayed for a variety of reasons, including difficulties and delays related to:

- obtaining regulatory approval to commence a clinical study;
- identifying appropriate study sites and reaching agreements with prospective study sites and investigators, on acceptable terms, which can be subject to extensive negotiation and may vary significantly among study sites;
- obtaining institutional review board, or IRB, approval to conduct a clinical study at a prospective site;
- reaching agreements with prospective contract research organizations, or CROs, for the conduct of clinical studies and contract manufacturing organizations, or CMOs, for the production of clinical trial material, the terms of which agreements can be subject to extensive negotiation and may vary significantly among different CROs and CMOs;
- failures on the part of our CROs, CMOs, and other third-party contractors in developing procedures and protocols or otherwise conducting activities in accordance with applicable policies and procedures and on timelines requested by us;
- identifying and hiring or engaging, as applicable, additional employees or consultants to assist us in managing CRO and/or CMO activities, managing a clinical study and analyzing the data resulting from a study;
- recruiting and enrolling patients to participate in a clinical study;

- manufacturing sufficient quantities of clinical trial material due, among other things, to lack of availability of capacity at a CMO or of the component materials, including the active pharmaceutical ingredient, or API;
- having patients complete a study and/or return for and complete post-treatment follow-up; and
- unforeseen results from other clinical studies or nonclinical testing that require us to amend a study design or halt or terminate a clinical study.

Patient enrollment, a critical component to successful completion of a clinical study, is affected by many factors, including the size and nature of the study subject population, the proximity of patients to clinical sites, the eligibility criteria for the study, the design of the clinical study, competing clinical studies and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to available alternatives, including therapies being investigated by other companies. Further, completion of a clinical study and/or its results may be adversely affected by failure to retain subjects who enroll in a study but withdraw due to adverse side effects, lack of efficacy, improvement in condition before treatment has been completed or for personal issues or who fail to return for or complete post-treatment follow-up.

In addition, a clinical study may be suspended or terminated by us, an IRB, a data safety monitoring board, the FDA or other regulatory authorities due to a number of factors, including:

- failure to conduct the study in accordance with regulatory requirements or the study's protocol;
- inspection of clinical study operations or sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- unforeseen safety issues, including adverse side effects;
- changes in governmental regulations or administrative actions; or
- lack of adequate funding to continue the study.

Changes in governmental regulations and guidance relating to clinical studies may occur and we may need to amend study protocols to reflect these changes, or we may amend study protocols for other reasons. Amendments may require us to resubmit protocols to IRBs for reexamination or renegotiate terms with CROs, study sites and investigators, all of which may adversely impact the costs or timing of or our ability to successfully complete a trial.

Clinical studies may not begin on time or be completed in the timeframes we anticipate and may be more costly than we anticipate for a variety of reasons, including one or more of those described above. For example, although we expect to move vepoloxamer directly into Phase 2 studies for most new indications we plan to pursue, an IRB or the FDA or another regulatory agency may require additional clinical or nonclinical studies prior to initiation of any planned Phase 2 study, which likely would increase the total time and cost of development in that indication. The length of time necessary to complete clinical studies varies significantly and is difficult to predict accurately. We may make statements regarding anticipated timing for completion of enrollment in and/or availability of results from our clinical studies, but such predictions are subject to a number of significant assumptions and actual timing may differ materially for a variety of reasons, including patient enrollment rates, length of time needed to prepare raw study data for analysis and then to review and analyze it, and other factors described above. In addition, in the case of AIR001, we are supporting but are not the sponsor of the ongoing Phase 2 clinical studies and, as a result, the initiation and completion of and receipt of data from those studies is outside of our control. If we experience delays in the completion of a clinical study, if a clinical study is terminated, or if failure to conduct a study in accordance with regulatory requirements or the study's protocol leads to deficient safety and/or efficacy data, the regulatory approval and/or commercial prospects for our product candidate may be harmed and our ability to generate product revenue will be delayed. In addition, any delays in completing our clinical studies likely will increase our development costs. Further, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may ultimately lead to the denial of regulatory approval of a product candidate. Even if we are able to ultimately commercialize our product candidates, other therapies for the same indications may be introduced to the market in the interim and establish a competitive advantage or diminish the need for our products.

We do not have, and do not have plans to establish, any manufacturing facilities and are dependent on third parties for the manufacture and supply of our product candidates, and the loss of any of these manufacturers, or their failure to provide us with an adequate supply of drug product in a timely manner and on commercially acceptable terms, or at all, could harm our business.

We do not have, and do not have plans to establish, our own manufacturing facilities. For clinical trial material, we have entered into supply agreements with third parties for both API and finished drug product, but our current agreements may not cover all of our clinical trial material needs and we may need to negotiate new or amended agreements with these CMOs or rely on individual proposals or statements of work, which inherently involves uncertainty as to ongoing supply and may result in delays in the completion of ongoing clinical studies or initiation of new studies. In addition, as development of our product candidates progress, we

will need to negotiate agreements for commercial supply, including with respect to vepoloxamer for patients with sickle cell disease; however, we may not be able to reach an agreement containing terms that are acceptable to us, or at all. If we fail to maintain relationships with our current CMOs, we may not be able to complete development of our product candidates, including vepoloxamer, or market them, if approved, on a timely basis, or at all, which would have a material and adverse effect on our business.

Third-party manufacturers and suppliers may not perform as agreed or may terminate their agreements with us. For example, because these third parties provide manufacturing services to a number of other pharmaceutical companies, they may experience capacity constraints or choose to prioritize one or more of their other customers over us. Any significant problem that our manufacturers or suppliers experience could delay or interrupt our supply of clinical trial material or commercial product until the manufacturer or supplier cures the problem or until we locate, negotiate for and validate an alternative source of supply, if one is available.

In addition to our reliance on third parties to manufacture clinical trial material, we rely on them to conduct or assist us in conducting key manufacturing development activities, including qualification of equipment, developing and validating methods, defining critical process parameters, releasing component materials and conducting stability testing, among other things. If these third parties are unable to perform successfully in a timely manner, whether for technical, financial or other reasons, we may be unable to secure clinical trial material, which likely would delay the initiation, conduct or completion of our clinical studies, which, in turn, likely would have a material and adverse effect on our business.

All manufacturers of our clinical trial material and, as applicable, commercial product, including API manufacturers, must comply with cGMP requirements enforced by the FDA through its facilities inspection program and applicable requirements of foreign regulatory authorities. These requirements include quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our clinical trial material may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. While we or our representatives generally monitor and audit our manufacturers' systems, we have little control over their ongoing compliance with these regulations. Failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval.

Currently, we do not have alternative sources to backup our primary sources of clinical trial material. Identification of and discussions with other vendors may be protracted and/or unsuccessful. Therefore, if our primary sources become unable or unwilling to perform, we could experience protracted delays or interruptions in the supply of clinical trial material and, ultimately, product for commercial sale, which could materially and adversely affect our development programs, commercial activities, operating results and financial condition. In addition, the FDA may require that we have an alternate manufacturer of our vepoloxamer drug product before approving it for marketing and sale in the U.S. and securing such alternate manufacturer before approval of an NDA for vepoloxamer could result in considerable additional time and cost prior to NDA approval.

If we are unable to maintain our relationship with our current supplier of vepoloxamer API, we may be unable to identify or establish a relationship with an alternate CMO that has the technical capabilities and desire to perform the development and supply services that we require for vepoloxamer on commercially reasonable terms, or at all. Production of vepoloxamer requires application of our proprietary fluid extraction process. This extraction process is complex and requires highly specialized equipment and there are a limited number of CMOs capable of performing and willing to perform the process as we require, which makes identifying and establishing relationships with CMOs more difficult and may provide them with leverage over us in any negotiations. In addition, we use commercially-available poloxamer 188 as API starting material. There are a limited number of sources of poloxamer 188, and we are not aware of any that currently manufacture it to cGMP requirements applicable to API. The current supplier of our starting material manufactures it under excipient-grade cGMP conditions. Prior to approval of any vepoloxamer-based product, the FDA or other regulatory agencies may require our starting material to be manufactured consistent with cGMP requirements applicable to API, in which case regulatory approval and commercialization of our product candidate could be delayed significantly and require substantial additional financial resources as we seek to contract with a third party to manufacture the starting material consistent with cGMP requirements applicable to API or undertake to manufacture it ourselves, and conduct any additional clinical or nonclinical activities with such material as the FDA may require. Even if the FDA accepts our current approach with respect to API starting material, we do not have any control over its production and the third-party supplier may change its manufacturing process and/or limit the availability of its poloxamer 188 product in the future. If we cannot reach an agreement with the supplier to establish quality assurance controls around the API starting material or if the supplier makes changes to its poloxamer 188 product, the FDA may determine that it is not acceptable API starting material and we may have difficulty obtaining an alternate supply of API starting material that the FDA finds acceptable without our conducting additional clinical or nonclinical activities or taking other remedial measures, which could require substantial time and financial resources. As a result, we could experience significant disruption in our ability to manufacture vepoloxamer, which likely would add significantly to its overall development and commercialization costs and adversely affect our business and financial condition.

Any new manufacturer or supplier of finished drug product or its component materials, including API, would be required to qualify under applicable regulatory requirements and would need to have sufficient rights under applicable intellectual property laws to the method of manufacturing such product or ingredients. The FDA may require us to conduct additional clinical studies, collect stability data and provide additional information concerning any new supplier, or change in a validated manufacturing process, including

scaling-up production, before we could distribute products from that manufacturer or supplier or revised process. For example, if we were to engage a third party other than our current CMO to supply vepoloxamer for future clinical trial material or commercial product, the FDA may require us to conduct additional clinical and nonclinical studies to ensure comparability of the drug substance manufactured by our current CMO to drug substance manufactured by the new supplier. In addition to the potential for such requirements to result in significant interruption to development and commercialization of vepoloxamer, we likely would incur substantial additional costs to comply with the additional requirements.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling-up initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, and shortages of qualified personnel. None of our product candidates has been manufactured at the scale we believe will be necessary to maximize its commercial value and, accordingly, we may encounter difficulties in attempting to scale-up production and may not succeed in that effort on a timely basis or at all, including as a result of delaying activities necessary to establish commercial-scale production due to capital constraints. In addition, the FDA or other regulatory authorities may impose additional requirements as we scale-up initial production capabilities, which may delay our scale-up activities or add expense.

If our manufacturers encounter any of these difficulties or otherwise fail to comply with their contractual obligations or we delay in entering into commercial supply agreements due to capital constraints, we may have insufficient quantities of material to support ongoing and/or planned clinical studies or to meet commercial demand for vepoloxamer, if approved. In addition, any delay or interruption in the supply of materials necessary or useful to manufacture our product candidates could delay the completion of our clinical studies, increase the costs associated with our development programs and, depending upon the period of delay, require us to commence new clinical studies at significant additional expense or terminate the studies completely. Delays or interruptions in the supply of commercial product could result in increased cost of goods sold and lost sales. We cannot ensure that manufacturing or quality control problems will not arise in connection with the manufacture of our clinical trial material or commercial product, if approved, or that third-party manufacturers will be able to maintain the necessary governmental licenses and approvals to continue manufacturing such clinical trial material or commercial product, as applicable. In addition, vepoloxamer currently is manufactured outside the U.S. and, as a result, we may experience interruptions in supply due to shipping or customs difficulties or regional instability. Any of the above factors could cause us to delay or suspend anticipated or ongoing trials, regulatory submissions or commercialization of our product candidates, entail higher costs or result in our being unable to effectively commercialize our products. Our dependence upon third parties for the manufacture of our clinical trial material may adversely affect our future costs and our ability to develop and commercialize our product candidates on a timely and competitive basis.

Positive results in nonclinical testing and prior clinical studies do not ensure that ongoing or future clinical studies will be successful or that our product candidates will receive the regulatory approvals necessary for their commercialization.

Before obtaining regulatory approval for the commercial sale of any of our product candidates, we must demonstrate through nonclinical testing and clinical studies that each product is safe and effective for use in each target indication. Based on extensive nonclinical testing, we believe we understand our product candidates' respective mechanisms of action; however, previously observed pharmacologic effects and clinical benefits may not be observed in ongoing or future nonclinical or clinical studies. Success in nonclinical testing and prior clinical studies does not ensure that subsequent or larger-scale studies will be successful. For example, poloxamer 188 (non-purified) was tested in more than 2,000 human subjects in various indications before its development was discontinued, principally due to concerns regarding acute renal dysfunction observed in patients who received it. In contrast, vepoloxamer was generally well-tolerated in seven completed clinical studies and the effects on serum creatinine reported as adverse events among subjects who received vepoloxamer were comparable to those among subjects who received placebo. However, patient safety concerns, including renal dysfunction, may be observed in ongoing or future clinical studies, including EPIC. With respect to efficacy, although there is encouraging data from nonclinical and clinical studies of poloxamer 188 and vepoloxamer in multiple indications, ongoing and future studies of vepoloxamer may fail to demonstrate clinical benefits to human subjects, or the demonstrated benefits may be judged by regulatory agencies as not clinically meaningful.

Clinical study results frequently are susceptible to varying interpretations. Medical professionals, investors and/or regulatory authorities may analyze or weigh study data differently than we do. For example, even if a study drug demonstrates a statistically significant treatment effect in its primary objective in a Phase 3 study, a regulatory agency could determine that the study data are not sufficient to support approval and require additional testing prior to granting approval. In addition, determining the value of clinical data typically requires application of assumptions and extrapolations to raw data. Alternative methodologies may lead to differing conclusions, including with respect to the safety or efficacy of our product candidates. For example, alternative methods for applying missing or imputed data may have impacted the treatment effect observed in the prior-sponsor Phase 3 study of vepoloxamer in sickle cell disease. If regulatory authorities disagree with us as to the appropriate methods for analyzing study data, regulatory approval for our product candidates may be delayed, limited or withheld.

If we license to third parties rights to develop our product candidates in other geographic areas or in other indications or otherwise permit third-parties to evaluate our product candidates in clinical studies, such as in the case of AIR001, we may have limited control

over nonclinical testing or clinical studies that may be conducted by such third-parties. If data from third-party testing identifies a safety or efficacy concern, it could adversely affect our or another licensee's development of the product candidate and prospects for regulatory approval.

There is significant risk that our product candidates could fail to show anticipated results in ongoing and future nonclinical testing and/or clinical studies, including the EPIC study, and, as a result, we may be required to conduct additional costly testing or we may elect to discontinue one or more of our development programs. A failure to obtain requisite regulatory approvals or to obtain approvals of the scope requested will delay or preclude us from marketing our products or limit the commercial use of the products, and would have a material adverse effect on our business, financial condition and results of operations.

We rely significantly on third parties to conduct our nonclinical testing and clinical studies and other aspects of our development programs and if those third parties do not satisfactorily perform their contractual obligations or meet anticipated deadlines, the development of our product candidates could be adversely affected.

We do not employ personnel or possess the facilities necessary to conduct many of the activities associated with our programs. We engage consultants, advisors, CROs, CMOs and others to assist in the design and conduct of nonclinical and clinical studies of our product candidates, with interpretation of the results of those studies and with regulatory activities, and we expect to continue to outsource a significant amount of such activities. As a result, many important aspects of our development programs are and will continue to be outside our direct control, and our third-party service providers may not perform as required or expected. Further, such third parties may not be as committed to the success of our programs as employees and, therefore, may not devote the same time, thoughtfulness or creativity to completing projects or problem-solving as would an employee. To the extent we are unable to successfully manage the performance of third-party service providers, our business may be adversely affected.

The CROs that we engage to execute our clinical studies play a significant role in the conduct of the studies, including the collection and analysis of study data, and we likely will depend on CROs and clinical investigators to conduct future clinical studies and to assist in analyzing data from completed studies and developing regulatory strategies for our product candidates. Individuals working at the CROs with which we contract, as well as investigators at the sites at which our studies are conducted, are not our employees, and we have limited control over the amount or timing of resources that they devote to our programs. With respect to our AIR001 program, AIR001 is being tested in third-party-sponsored clinical studies and, because we are not the study sponsor, our control over these studies is further limited. If our CROs and/or study investigators fail to devote sufficient time and resources to studies of our product candidates, if they do not comply with all regulatory and contractual requirements, or if their performance is substandard, it may delay commencement and/or completion of these studies, submission of our new drug applications to the FDA and other regulatory agencies, approval of our applications by those agencies, and commercialization of our products. Failure of these CROs to meet their obligations could adversely affect development of our product candidates. For example, in 2006, we engaged a CRO to assist with the primary conduct of our bioequivalence study of Exelbine, including monitoring participating clinical sites to ensure compliance with regulatory requirements. FDA guidance recommends that clinical sites randomly select and retain reserve samples of study drugs used in bioequivalence studies. However, the clinical sites that participated in our bioequivalence study of Exelbine failed to do so. In August 2011, we received a complete response letter from the FDA stating that the authenticity of the study drugs used in that bioequivalence study could not be verified and, consequently, the study would need to be repeated to address that deficiency.

In addition, CROs we engage may have relationships with other commercial entities, some of which may compete with us. If they assist our competitors at our expense, it could harm our competitive position. Moreover, if any of our current CRO relationships were to terminate, particularly those with the CROs we have engaged to conduct the EPIC study, we may not be able to enter into arrangements with alternative CROs on acceptable terms or in a timely manner, or at all. Switching CROs would involve additional cost and divert management time and attention. In addition, there likely would be a transition period when a new CRO commences work. These challenges could result in delays in the commencement or completion of our clinical studies, which could materially impact our ability to meet our desired development timelines and have a material adverse impact on our business and financial condition.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their clinical development, regulatory approval or commercialization.

Undesirable side effects caused by our product candidates could interrupt, delay or halt clinical studies and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all indications, and in turn prevent us from commercializing our product candidates. For example, while we believe our proprietary purification process has addressed the cause of the acute renal dysfunction observed in clinical studies of poloxamer 188 (non-purified), we cannot provide assurance that the purification process has fully addressed the issue or that renal toxicity will not be observed in ongoing or future studies of vepoloxamer, particularly if we conduct studies in patients with impaired renal function. In addition, transient, generally mild to moderate elevations in liver enzymes were associated with treatment with vepoloxamer in prior clinical studies. If in our clinical studies of vepoloxamer we observe more pronounced increases in liver enzymes, or we observe other previously unidentified adverse events, whether or not statistically significant, we may be required to conduct additional clinical studies of vepoloxamer or to investigate the clinical significance of the adverse event and vepoloxamer may not receive regulatory approval.

If any of our product candidates receive marketing approval and we or others later identify undesirable side effects caused by the product or, if applicable, the reference product:

- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- regulatory authorities may withdraw their approval of the product;
- we may be required to change the way the product is administered, conduct additional clinical studies or change the labeling of the product; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase the costs and expenses of commercializing the product, which in turn could delay or prevent us from generating significant revenue from its sale.

We may not achieve our projected development goals in the time frames we announce.

We set goals for and make public statements regarding our estimates of the timing for accomplishing certain objectives material to successful development of our product candidates. The actual timing of these events can vary, sometimes dramatically, due to many factors, including delays or failures in our nonclinical testing, clinical studies and manufacturing and regulatory activities and the uncertainties inherent in the regulatory approval process. For example, we had expected to initiate the EPIC study in 2012, but unforeseen delays related to the manufacture of clinical trial material delayed initiation of the study to 2013. In addition, from time to time we estimate the timeframe for completion of enrollment of or announcement of data from our clinical studies. However, predicting the rate of enrollment or the time from completion of enrollment to announcement of data for any clinical study, including EPIC, requires us to make a number of significant assumptions that may prove to be incorrect. If, as a clinical study progresses, we gain reliable information that materially impacts our assumptions, we will adjust our estimates. Even so, as discussed in other risk factors above, our estimated enrollment rates and the actual rates may differ materially and the time required to complete enrollment of any clinical study may be considerably longer than we estimate. In addition, even if we complete enrollment as expected, it may take longer than anticipated to prepare the data for review and then to review, analyze and announce the data.

Even if we complete a clinical study with successful results, we may not achieve our projected development goals in the time frames we initially anticipate or announce. As discussed above, the FDA may require nonclinical testing and/or clinical studies prior to its review or approval of a NDA for vepoloxamer in sickle cell disease in addition to the EPIC study and the other testing that we are conducting. If a development plan for a product candidate becomes more extensive and costly than anticipated, we may determine that the associated time and cost are not financially justifiable and, as a result, discontinue development in a particular indication or of the product candidate as a whole. Any such action may be viewed negatively, which could adversely affect our stock price.

In addition, changes may occur in regulatory requirements or policy during the period of product development and/or regulatory review of an NDA that relate to the data required to be included in NDAs. For example, despite including in our initial Exelbine NDA submission in December 2009 data that we believe met the filing requirements for a new drug promulgated by the International Conference on Harmonization, or ICH, as well as site-specific stability data from lots manufactured at the intended commercial manufacturing site, we received a refusal-to-file letter from the FDA indicating that the data included in that submission was insufficient to support a commercially-viable expiration dating period. Consequently, we had to generate 12 months of stability data from material manufactured at our intended commercial manufacturing site before resubmitting the Exelbine NDA, which we did in November 2010. A change in regulatory policy, which may not have been formalized or publicly disseminated, may have been a factor underlying the FDA's refusal to file our December 2009 submission.

Further, throughout development, we must provide adequate assurance to the FDA and other regulatory authorities that we can consistently produce our product candidates in conformance with cGMP and other regulatory standards. As discussed above, we rely on CMOs for the manufacture of clinical, and future commercial, quantities of our product candidates. If future FDA or other regulatory authority inspections identify cGMP compliance issues at these third-party facilities, production of our clinical trial material or, in the future, commercial product, could be disrupted, causing potentially substantial delay in development or commercialization of our product candidates.

Even if we receive regulatory approval for a product candidate, we may face development and regulatory difficulties that could materially and adversely affect our business, financial condition and results of operations and cause our stock price to decline.

Even if initial regulatory approval is obtained, or as a condition to the initial approval, the FDA or a foreign regulatory agency may impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies or marketing surveillance programs, any of which would limit the commercial potential of the product. Our product

candidates also will be subject to ongoing FDA requirements related to the manufacturing processes, labeling, packaging, storage, distribution, advertising, promotion, record-keeping and submission of safety and other post-market information regarding the product. For instance, the FDA may require changes to approved drug labels, require post-approval clinical studies and impose distribution and use restrictions on certain drug products. In addition, approved products, manufacturers and manufacturers' facilities are subject to continuing regulatory review and periodic inspections. If previously unknown problems with a product are discovered, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, the FDA may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we or a CMO of ours fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend or terminate any ongoing clinical studies;
- refuse to approve pending applications or supplements to approved applications;
- exclude our product from reimbursement under government healthcare programs, including Medicaid or Medicare;
- impose restrictions or affirmative obligations on our or our CMO's operations, including costly new manufacturing requirements;
- close the facilities of a CMO; or
- seize or detain products or require a product recall.

Even though we have obtained orphan drug designation for vepoloxamer for the treatment of sickle cell disease, we may not be able to obtain orphan drug marketing exclusivity for our products.

Vepoloxamer has orphan drug designation from the FDA and the European Commission for the treatment of sickle cell disease. 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 multi-year period of marketing exclusivity, which precludes the FDA or the European Commission from approving another marketing application for the same drug for that time period. However, orphan drug marketing exclusivity may not effectively protect our product candidates, even if our product candidates are the first to receive regulatory approval for the rare disease or condition. The FDA can subsequently approve another drug or biologic for the same indication if the FDA concludes that the competing product is clinically superior (safer and/or more effective) or makes a major contribution to patient care. The European Commission may reduce the exclusivity period in the EU 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. Further, orphan drug exclusivity may be lost if the FDA or European Commission determines that the request for designation was materially defective or if the manufacturer of the drug is unable to assure a quantity of the drug sufficient to meet the needs of patients with the rare disease or condition. In addition, orphan drug designation does not shorten the regulatory review process for obtaining marketing approval.

Even though vepoloxamer has FDA fast track designation for the treatment of vaso-occlusive crisis of sickle cell disease, we may not experience a faster regulatory review process.

The FDA has granted vepoloxamer fast track designation for the treatment of vaso-occlusive crisis of sickle cell disease. For a product candidate with track designation, the FDA may agree to more frequent interactions with us during our development of vepoloxamer and to initiate review of sections of an NDA before the application is complete, which could expedite the FDA review process for granting marketing approval. However, fast track designation does not guarantee that the FDA will agree to this "rolling review" process. In addition, the FDA may withdraw a drug's fast track designation if it determines that the drug no longer demonstrates a potential to address unmet medical need or is not being studied in a manner that shows the drug can treat a serious condition and meets an unmet medical need. A drug may no longer demonstrate a potential to address unmet medical need, for example, if the FDA approved a different product that addressed the same need or if emerging clinical data failed to show that the drug with fast track designation had the anticipated advantage over an available therapy. In spite of vepoloxamer's fast track designation, ultimately, the FDA may not agree to a rolling review process for an NDA for vepoloxamer for the treatment of vaso-occlusive crisis of sickle cell disease. In addition, although there are no approved therapies for the treatment of an ongoing vaso-occlusive crisis in sickle cell disease and our vepoloxamer NDA may be eligible for priority review, the FDA may determine to review our NDA on a standard review basis.

We have never commercialized a product candidate and we may lack the necessary expertise, personnel and resources to successfully commercialize any of our product candidates that receive regulatory approval on our own or together with suitable partners, which could delay and/or limit our ability to generate revenue in the event we receive regulatory approval to market one of our product candidates.

Our operations to date have been limited to business planning, raising capital, acquiring our product candidates and nonclinical and clinical development of our product candidates. We have never commercialized a product candidate and currently have limited marketing capabilities and no sales force or distribution capabilities. To achieve commercial success of our vepoloxamer product candidate or any other product candidate, if approved, we will have to develop our own marketing, distribution, sales and associated regulatory compliance capabilities, or outsource one or more of these activities to a third party. There is no guarantee that we will be able to establish adequate marketing, distribution or sales capabilities or make arrangements with third parties to perform those activities on terms satisfactory to us, or at all, or that any internal capabilities or third-party arrangements will be cost-effective.

Factors that may affect our ability to commercialize our product candidates on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, obtaining access to or persuading adequate numbers of physicians to prescribe our product candidates and other unforeseen expenses, difficulties, complications and delays associated with building an independent sales and marketing organization. Developing commercialization and associated regulatory compliance capabilities requires substantial investment, is time consuming, and could delay launch of any product candidate for which we receive regulatory approval. We may not be able to build an effective sales and marketing organization in the United States, the European Union or other key global markets in which our product candidates may be approved. If we are unable to build our own marketing, sales or distribution capabilities or to find suitable third parties to perform these activities for us, the launch of an approved product may be delayed and we may not generate revenues from them in the timeframes in which we expect, or at all.

To the extent we outsource marketing, distribution or sales activities to third parties, those third parties may hold significant control over important aspects of the commercialization of our products, including market identification, marketing methods, pricing, composition of sales force and promotional activities. Even if we are successful in establishing and maintaining these arrangements, there can be no assurance that we will be able to control the amount and timing of resources that any third party may devote to our products or prevent any third party from pursuing alternative technologies or products that could result in the development of products that compete with, or the withdrawal of support for, our products. If we retain third-party service providers to perform functions related to the marketing, distribution and sale of our products, key aspects of those functions that may be out of our direct control could include warehousing and inventory management, distribution, contract administration and chargeback processing, accounts receivable management and call center management. In this event, we would place substantial reliance on third-party providers to perform services for us, including entrusting our inventories of products to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, encounter natural or other disasters at their facilities or otherwise fail to perform in a satisfactory manner, or at all, our ability to deliver product to meet commercial demand could be significantly impaired. In addition, we may use third parties to perform various other services for us relating to sample accountability and regulatory monitoring, including adverse event reporting, safety database management and other product maintenance services. If the quality or accuracy of the data maintained by these service providers is insufficient, our ability to continue to market our products could be jeopardized or we could be subject to regulatory sanctions.

If any of our product candidates for which we receive regulatory approval fails to achieve significant market acceptance among the medical community, patients or third-party payors, the revenue we generate from its sales will be limited and our business may not be profitable.

Our success will depend in substantial part on the extent to which our product candidates, if approved, are accepted by the medical community and patients and reimbursed by third-party payors, including government payors. The degree of market acceptance with respect to each of our approved products, if any, will depend upon a number of factors, including:

- the safety and efficacy of our product demonstrated in clinical studies;
- acceptance in the medical and patient communities of our product as a safe and effective treatment;
- the perceived advantages of our product over alternative treatments, including with respect to the incidence and severity of any adverse side effects and the cost of treatment;
- the indications for which our product is approved;
- claims or other information (including limitations or warnings) in our product's approved labeling;
- reimbursement and coverage policies of government and other third-party payors;
- pricing and cost-effectiveness of our product relative to alternative treatments;

- availability of alternative treatments;
- the prevalence of off-label substitution of chemically equivalent products or alternative treatments; and
- the resources we devote to marketing our product and restrictions on promotional claims we can make with respect to the product.

We cannot predict with reasonable accuracy whether physicians, patients, healthcare insurers or health maintenance organizations, or the medical community in general, will accept or utilize any of our products. If our product candidates are approved but do not achieve an adequate level of acceptance by these parties, we may not generate sufficient revenue to become or remain profitable. In addition, our efforts to educate the medical community and third-party payors regarding benefits of our products may require significant resources and may never be successful.

If we determine that a product candidate may not achieve adequate market acceptance or that the potential market size does not justify additional expenditure on the program, we may reduce our expenditures on the development and/or the process of seeking regulatory approval of the product candidate while we evaluate whether and on what timeline to move the program forward.

Even if we receive regulatory approval to market one or more of our product candidates in the U.S., we may never receive approval or commercialize our products outside of the U.S., which would limit our ability to realize the full commercial potential of our product candidates.

In order to market any products outside of the U.S., we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks detailed above regarding FDA approval in the U.S., as well as other risks. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects detailed above regarding FDA approval in the U.S. As described above, such effects include the risks that our product candidates may not be approved for all indications requested, which could limit the uses of our product candidates and have an adverse effect on product sales, and that such approval may be subject to limitations on the indicated uses for which the product may be marketed or require costly, post-marketing follow-up studies.

Risks Related to Our Intellectual Property

Our success will depend in part on obtaining and maintaining effective patent and other intellectual property protection for our product candidates and proprietary technology.

Our success will depend in part on our ability to:

- obtain and maintain patent and other exclusivity with respect to our products and their use;
- prevent third parties from infringing upon our proprietary rights;
- maintain proprietary know-how and trade secrets;
- operate without infringing upon the patents and proprietary rights of others; and
- obtain appropriate licenses to patents or proprietary rights held by third parties if infringement would otherwise occur or if necessary to secure exclusive rights to them, both in the U.S. and in foreign countries.

The patent and intellectual property positions of biopharmaceutical companies generally are highly uncertain, involve complex legal and factual questions, and have been and continue to be the subject of much litigation. There is no guarantee that we have or will develop or obtain the rights to products or processes that are patentable, that patents will issue from any pending applications or that claims allowed will be sufficient to protect the technology we develop or have developed or that is used by us, our CMOs or our other service providers. In addition, any patents that are issued to us may be limited in scope or challenged, invalidated, infringed or circumvented, including by our competitors, and rights we have under issued patents may not provide competitive advantages to us. If competitors can develop and commercialize technology and products similar to ours, our ability to successfully commercialize our technology and products may be impaired.

Patent applications in the U.S. are confidential for a period of time until they are published, and publication of discoveries in scientific or patent literature typically lags actual discoveries by several months. As a result, we cannot be certain that the inventors listed in any patent or patent application owned by us were the first to conceive of the inventions covered by such patents and patent applications

(for U.S. patent applications filed before March 16, 2013), or that such inventors were the first to file patent applications for such inventions outside the United States and, after March 15, 2013, in the United States. In addition, changes in or different interpretations of patent laws in the United States and foreign countries may affect our patent rights and limit the number of patents we can obtain, which could permit others to use our discoveries or to develop and commercialize our technology and products without any compensation to us.

We also rely on unpatented know-how and trade secrets and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, through confidentiality agreements with employees, consultants, collaborators and others. We also have invention or patent assignment agreements with our employees and certain consultants. The steps we have taken to protect our proprietary rights, however, may not be adequate to preclude misappropriation of or otherwise protect our proprietary information or prevent infringement of our intellectual property rights, and we may not have adequate remedies for any such misappropriation or infringement. In addition, it is possible that inventions relevant to our business could be developed by a person not bound by an invention assignment agreement with us or independently discovered by a competitor.

We also intend to rely on regulatory exclusivity for protection of our product candidates, if approved for commercial sale. Implementation and enforcement of regulatory exclusivity, which may consist of regulatory data protection and market protection, varies widely from country to country. Failure to qualify for regulatory exclusivity, or failure to obtain or maintain the extent or duration of such protections that we expect for our product candidates, if approved, could affect our decision on whether to market the products in a particular country or countries or could otherwise have an adverse impact on our revenue or our results of operations.

We may rely on trademarks, trade names and brand names to distinguish our products, if approved for commercial sale, from the products of our competitors. However, our trademark applications may not be approved. Third parties may also oppose our trademark applications or otherwise challenge our use of the trademarks in which case we may expend substantial resources to defend our trademarks and may enter into agreements with third parties that may limit our use of our trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our product, which could result in loss of brand recognition and could require us to devote significant resources to advertising and marketing these new brands. Further, our competitors may infringe our trademarks or we may not have adequate resources to enforce our trademarks.

Our success depends in large part on our ability to prevent competitors from duplicating or developing equivalent versions of our product candidates, but patent protection, including for vepoloxamer, may be difficult to obtain and any issued claims may be limited.*

The potential therapeutic benefits of poloxamer 188 have been known for decades and there is substantial prior art describing compositions of poloxamer 188, including purified poloxamer 188, and their uses in a wide range of diseases and conditions. As a result, our ability to find novel and non-obvious uses of vepoloxamer is limited. Further, a patent examiner may combine numerous, disparate references in order to reject a claimed composition, formulation and/or use for obviousness. If the prior art suggests, even implicitly, the desirability of combining previously known elements, such as the use of poloxamer 188 in a particular indication, the subsequent use of vepoloxamer in that indication may be unpatentable.

We have filed for patent protection of vepoloxamer as a novel composition of poloxamer material as well as to cover various methods of therapeutic use of poloxamers, including vepoloxamer. However, our pending patent applications may not issue as patents, any issued patents may not provide us with significant competitive advantages, the validity or enforceability of any of our patents may be challenged and, if instituted, one or more of these challenges may be successful. For instance, our patent covering a purportedly novel composition of poloxamer material, methods of use and process of manufacture may be challenged in the U.S. under post-grant review proceedings, *inter partes* reexamination, *ex parte* re-examination, or challenges in district court. Any similar patents issued in foreign jurisdictions may be subjected to comparable proceedings lodged in various foreign patent offices. These proceedings could result in either loss of the patent or loss or reduction in the scope of one or more of the claims of the patent. Even if a patent issues, and is held valid and enforceable, competitors may be able to design around our patents, such as by using pre-existing or newly developed technology, in which case competitors may not infringe our issued claims and may be able to market and sell products that compete directly with ours before our patents expire.

The patent prosecution process is expensive and time-consuming. We and any future licensors and licensees may not apply for or prosecute patents on certain aspects of our product candidates at a reasonable cost, in a timely fashion, or at all. We may not have the right to control the preparation, filing and prosecution of some patent applications related to our product candidates or technologies. As a result, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our company. It is also possible that we or any future licensors or licensees will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Further, it is possible that defects of form in the preparation or filing of our patent applications may exist, or may arise in the future, such as with respect to proper priority claims, inventorship, assignment, or claim scope. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid or unenforceable. In addition, one or more parties may independently develop similar technologies or methods, duplicate our technologies or methods, or design around the patented aspects

of our products, technologies or methods. Any of these circumstances could impair our ability to protect our products, if approved, in ways which may have an adverse impact on our business, financial condition and operating results.

Furthermore, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in and outside of the United States. Such challenges 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 or identical products or technology, or limit the duration of the patent protection of our technology and drugs. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

Enforcement of intellectual property rights in countries outside the U.S., including China in particular, has been limited or non-existent. Future enforcement of patents and proprietary rights in many other countries will likely be problematic or unpredictable. Moreover, the issuance of a patent in one country does not assure the issuance of a similar patent in another country. Claim interpretation and infringement laws vary by nation, so the extent of any patent protection is uncertain and may vary in different jurisdictions.

Obtaining and maintaining our 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.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications are required to be paid to the U.S. Patent and Trademark Office, or USPTO, and various governmental patent agencies outside of the U.S. in several stages over the lifetime of the patents and applications. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after a patent has issued. There are situations in which non-compliance can result in decreased patent term adjustment or in abandonment or lapse of the patent or patent application, leading to partial or complete loss of patent rights in the relevant jurisdiction.

If we are sued for infringing the proprietary rights of third parties or our patents rights are otherwise challenged in administrative proceedings, defending such actions may be costly and time consuming, and an unfavorable outcome would have an adverse effect on our business.

Our commercial success depends on our ability and the ability of our CMOs and component suppliers to develop, manufacture, market and sell our products and product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are or may be developing products. As the industries in which we operate (biopharmaceutical, specialty pharmaceutical, biotechnology and pharmaceutical) expand and more patents are issued, the risk increases that we will be subject to claims that our products or product candidates, or their use or manufacture, infringe the rights of others. Because patent applications can take many years to publish and issue, there currently may be pending applications, unknown to us, that may later result in issued patents that our products, product candidates or technologies infringe, or that the process of manufacturing our products or any of their respective component materials, or the component materials themselves, infringe, or that the use of our products, product candidates or technologies infringe.

We or our CMOs or component material suppliers may be exposed to, or threatened with, litigation by third parties alleging that our products, product candidates and/or technologies infringe their patents and/or other intellectual property rights, or that one or more of the processes for manufacturing our products or any of their respective component materials, or the component materials themselves, or the use of our products, product candidates or technologies, infringe their patents and/or other intellectual property rights. If a third-party patent or other intellectual property right is found to cover our products, product candidates, technologies or their uses, or any of the underlying manufacturing processes or components, we could be required to pay damages and could be unable to commercialize our products or use our technologies or methods unless we are able to obtain a license to the patent or intellectual property right. A license may not be available to us in a timely manner or on acceptable terms, or at all. In addition, during litigation, the third-party alleging infringement could obtain a preliminary injunction or other equitable remedy that could prohibit us from making, using, selling or importing our products, technologies or methods.

There generally is a substantial amount of litigation involving patent and other intellectual property rights in the industries in which we operate and the cost of such litigation may be considerable. We can provide no assurance that our product candidates or technologies will not infringe patents or rights owned by others, licenses to which might not be available to us in a timely manner or on acceptable terms, or at all. If a third party claims that we or our CMOs or component material suppliers infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims which, with or without merit, may be expensive and time consuming to litigate and may divert our management's time and attention from our core business;

- substantial damages for infringement, including the potential for treble damages and attorneys' fees, which we may have to pay if it is determined that the product and/or its use at issue infringes or violates the third party's rights;

- a court prohibiting us from selling or licensing the product unless the third-party licenses its intellectual property rights to us, which it may not be required to do;

- if a license is available from the third party, we may have to pay substantial royalties, fees and/or grant cross-licenses to the third party; and

- redesigning our products or processes so they do not infringe, which may not be possible or may require substantial expense and time.

No assurance can be given that patents do not exist, have not been filed, or could not be filed or issued, which contain claims covering our products, product candidates or technology or those of our CMOs or component material suppliers or the use of our products, product candidates or technologies. Because of the large number of patents issued and patent applications filed in the industries in which we operate, there is a risk that third parties may allege they have patent rights encompassing our products, product candidates or technologies, or those of our CMOs or component material suppliers, or uses of our products, product candidates or technologies.

In addition, it may be necessary for us to enforce our proprietary rights, or to determine the scope, validity and unenforceability of other parties' proprietary rights, through litigation or other dispute proceedings, which may be costly, and to the extent we are unsuccessful, adversely affect our rights. In these proceedings, a court or administrative body could determine that our claims, including those related to enforcing patent rights, are not valid or that an alleged infringer has not infringed our rights. The uncertainty resulting from the mere institution and continuation of any patent- or other proprietary rights-related litigation or interference proceeding could have a material and adverse effect on us.

RISKS RELATED TO OUR INDUSTRY

We expect intense competition in the marketplace for our product candidates, should any of them receive regulatory approval.

The industries in which we operate (biopharmaceutical, specialty pharmaceutical, biotechnology and pharmaceutical) are highly competitive and subject to rapid and significant change. We are aware of many other organizations developing drug products and other therapies intended to treat or cure the diseases or conditions in which we are developing or plan to develop our product candidates. Developments by others may render potential application of any of our product candidates in a particular indication obsolete or noncompetitive, even prior to completion of its development and approval for that indication. If successfully developed and approved, we expect our product candidates will face intense competition. We may not be able to compete successfully against organizations with competitive products, particularly large pharmaceutical companies. Many of our potential competitors have significantly greater financial, technical and human resources than we do, and may be better equipped to develop, manufacture, market and distribute products. Many of these companies operate large, well-funded research, development and commercialization programs, have extensive experience in nonclinical and clinical studies, obtaining FDA and other regulatory approvals and manufacturing and marketing products, and have multiple products that have been approved or are in late-stage development. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical and biotechnology companies. Furthermore, heightened awareness on the part of academic institutions, government agencies and other public and private research organizations of the potential commercial value of their inventions have led them to actively seek to commercialize the technologies they develop, which increases competition for investment in our programs. In addition, there is increasing interest in developing drugs for rare diseases, which may have the effect of increasing the development of agents to treat sickle cell disease and other orphan indications we may pursue. Legislative action may generate further interest. Competitive products may be more effective, or more effectively marketed and sold, than ours, which would have a material adverse effect on our ability to generate revenue.

With respect to competition for vepoloxamer in sickle cell disease, we are aware of numerous companies with product candidates in varying stages of development for the prevention and treatment of vaso-occlusive crisis, including mechanisms that target the P2Y12 ADP receptor, increase oxygen binding of hemoglobin or stimulate production of fetal hemoglobin. Some of these companies are large, well-financed and experienced pharmaceutical and biotechnology companies or have partnered with such companies, which may give them development, regulatory and/or marketing advantages over us. For example, Pfizer and Novartis have each invested in companies, GlycoMimetics, Inc. and Selexys Pharmaceuticals Corporation, respectively, with clinical-stage agents for the treatment of vaso-occlusive crisis. Pfizer is enrolling a Phase 3 clinical study of GlycoMimetics' rivipansel in adult and adolescent patients with sickle cell disease experiencing vaso-occlusive crisis and estimates completion of the study in July 2018. Global Blood Therapeutics Inc. is conducting what it characterizes as a Phase 1/2 clinical study of its product candidate GBT440, an oral, once-daily therapy intended to prevent the sickling of red blood cells in sickle cell patients, and estimates completion of this early stage study in May

2016. Emmaus Life Sciences, Inc. has announced its plans to submit an NDA to the FDA in the summer of 2016 for marketing approval of its L-glutamine treatment for patients with sickle cell disease. Further, numerous non-profit or non-commercial foundations and interest groups are committed to improving outcomes for patients with sickle cell disease. Advances in the understanding of the signaling pathways associated with sickle cell disease may lead to further interest and development of treatment options. Forms of gene therapy are being pursued to correct sickle cell disease by halting production of sickled cells. For example, bluebird bio, Inc. is in Phase 1 development of its LentiGlobin® BB305 drug product for patients with severe sickle cell disease. If an effective treatment or cure for vaso-occlusive crisis or sickle cell disease receives regulatory approval, the potential commercial success of vepoloxamer could be severely jeopardized.

We are subject to uncertainty relating to healthcare reform measures and reimbursement policies that, if not favorable to our products, could hinder or prevent our products' commercial success, if any of our product candidates are approved.

The unavailability or inadequacy of third-party payor coverage and reimbursement could negatively affect the market acceptance of our product candidates and the future revenues we may expect to receive from those products. The commercial success of our product candidates, if approved, will depend in part on the extent to which the costs of such products will be covered by third-party payors, such as government health programs, commercial insurance and other organizations. These third-party payors are increasingly challenging the prices and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our products after approval as a benefit under their plans or, even if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis. In the case of products administered in an inpatient hospital setting, a level of payment that is inadequate to cover the cost to hospitals of providing and administering our products to patients, could delay market acceptance of or limit our ability to penetrate the markets for our products.

Significant uncertainty exists as to the reimbursement status for newly approved drug products, including coding, coverage and payment. There is no uniform policy requirement for coverage and reimbursement for drug products among third-party payors in the United States, therefore coverage and reimbursement for drug products can differ significantly from payor to payor. The coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate payment will be applied consistently or obtained. The process for determining whether a payor will cover and how much it will reimburse a product may be separate from the process of seeking approval of the product or for setting the price of the product. Even if reimbursement is provided, market acceptance of our products may be adversely affected if the amount of payment for our products proves to be unprofitable for healthcare providers or less profitable than alternative treatments or if administrative burdens make our products less desirable to use. Third-party payor reimbursement to providers of our products, if approved, may be subject to a bundled payment that also includes the procedure of administering our products. To the extent there is no separate payment for our product(s), there may be further uncertainty as to the adequacy of reimbursement amounts.

The continuing efforts of the government, private insurance companies, and other organizations to contain or reduce costs of healthcare may adversely affect:

- our ability to set an appropriate price for our products;
- the rate and scope of adoption of our products by healthcare providers;
- our ability to generate revenue or achieve or maintain profitability;
- the future revenue and profitability of our potential customers, suppliers and collaborators; and
- our access to additional capital.

Our ability to successfully commercialize our products will depend in part on the extent to which governmental authorities, private health insurers and other organizations establish what we believe are appropriate coverage and reimbursement for our products. The containment of healthcare costs has become a priority of federal and state governments and the prices of drug products have been a focus in this effort. For example, there have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. We expect that federal, state and local governments in the U.S. will continue to consider legislation directed at lowering the total cost of healthcare. In addition, in certain foreign markets, the pricing of drug products is subject to government control and reimbursement may in some cases be unavailable or insufficient. It is uncertain whether and how future legislation, whether domestic or abroad, could affect prospects for our product candidates or what actions federal, state, or private payors for healthcare treatment and services may take in response to any such healthcare reform proposals or legislation. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures reforms may prevent or limit our ability to generate revenue, attain profitability or commercialize our product candidates.

We face potential product liability exposure and, if successful claims are brought against us, we may incur substantial liability for a product or product candidate and may have to limit its commercialization. In the future, we anticipate that we will need to obtain additional or increased product liability insurance coverage and it is uncertain whether such increased or additional insurance coverage can be obtained on commercially reasonable terms, if at all.

Our business (in particular, the use of our product candidates in clinical studies and the sale of any products for which we obtain marketing approval) will expose us to product liability risks. Product liability claims might be brought against us by patients, healthcare providers, pharmaceutical companies or others selling our products. If we cannot successfully defend ourselves against any such claims, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our products and loss of revenue;
- impairment of our business reputation;
- delays in enrolling patients to participate in our clinical studies;
- withdrawal of clinical study participants;
- a "clinical hold," suspension or termination of a clinical study or amendments to a study design;
- significant costs of related litigation;
- substantial monetary awards to patients or other claimants; and
- the inability to commercialize our products and product candidates.

We maintain limited product liability insurance for our clinical studies, but our insurance coverage may not reimburse us or may not be sufficient to reimburse us for all expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses.

We expect that we will expand our insurance coverage to include the sale of commercial products if we obtain marketing approval of any of our product candidates, but we may be unable to obtain product liability insurance on commercially acceptable terms or may not be able to maintain such insurance at a reasonable cost or in sufficient amounts to protect us against potential losses. Large judgments have been awarded in class action lawsuits based on drug products that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

RISKS RELATED TO OUR COMMON STOCK

If we are unable to maintain compliance with NYSE MKT continued listing standards, our common stock may be delisted from the NYSE MKT equities market, which would likely cause the liquidity and market price of our common stock to decline.*

Our common stock currently is listed on the NYSE MKT equities market. The NYSE MKT will consider suspending dealings in, or delisting, securities of an issuer that does not meet its continued listing standards, including specified stockholders' equity levels. In addition, the NYSE MKT will consider suspending dealings in, or delisting, securities selling for a substantial period of time at a low price per share if the issuer fails to effect a reverse split of such stock within a reasonable time after being notified that the NYSE MKT deems such action to be appropriate under the circumstances.

In the past, though not since 2010, we were notified of non-compliance with certain NYSE MKT stockholders' equity continued listing standards; specifically, (1) Section 1003(a)(ii) of the NYSE MKT Company Guide, or the Company Guide, because we reported stockholders' equity of less than $4,000,000 and losses from continuing operations and net losses in three of our four most recent fiscal years, and (2) Section 1003(a)(iii) of the Company Guide, because we reported stockholders' equity of less than $6,000,000 and losses from continuing operations and net losses in our five most recent fiscal years. In addition, we were notified, in accordance with Section 1003(f)(v) of the Company Guide, that the NYSE MKT determined it was appropriate for us to effect a reverse stock split of our common stock to address our low selling price per share. In April 2010, we announced that we had resolved the stockholders' equity continued listing deficiencies and we implemented a 1-for-25 reverse split of our common stock, in part to address the NYSE MKT's requirement that we address our low stock price.

There is no assurance, however, that we will continue to maintain compliance with NYSE MKT continued listing standards. As of June 30, 2016, our stockholders' equity was $16.4 million. If we are unable to raise additional capital in 2016, our stockholders' equity could fall below the level required to maintain compliance with NYSE MKT continued listing standards. In addition, the market price for our common stock historically has been highly volatile, as more fully described below under the risk titled "The

market price of our common stock historically has been and likely will continue to be highly volatile." The NYSE MKT may again determine that the selling price per share of our common stock is low and require that we effect a reverse stock split of our common stock, which would require stockholder approval that we may be unable to obtain. Our failure to maintain compliance with NYSE MKT continued listing standards could result in the delisting of our common stock from the NYSE MKT.

The delisting of our common stock from the NYSE MKT likely would reduce the trading volume and liquidity in our common stock and may lead to decreases in the trading price of our common stock and may also materially impair our stockholders' ability to buy and sell shares. In addition, the delisting of our common stock could significantly impair our ability to raise additional capital, which we expect will be required in order to execute our current business strategy.

If our common stock were delisted and determined to be a "penny stock," a broker-dealer may find it more difficult to trade our common stock and an investor may find it more difficult to acquire or dispose of our common stock in the secondary market.

If our common stock were removed from listing with the NYSE MKT, it may be subject to the so-called "penny stock" rules. The SEC has adopted regulations that define a "penny stock" to be any equity security that has a market price per share of less than $5.00, subject to certain exceptions, such as any securities listed on a national securities exchange. For any transaction involving a "penny stock," unless exempt, the rules impose additional sales practice requirements on broker-dealers, subject to certain exceptions. If our common stock were delisted and determined to be a "penny stock," a broker-dealer may find it more difficult to trade our common stock and an investor may find it more difficult to acquire or dispose of our common stock on the secondary market.

The market price of our common stock historically has been and likely will continue to be highly volatile.

The market price for our common stock historically has been highly volatile, and the market for our common stock has from time to time experienced significant price and volume fluctuations, based both on our operating performance and for reasons that appear to us unrelated to our operating performance. For instance, the market price for our common stock dropped approximately 45% following our announcement of an underwritten public offering of equity securities on February 9, 2016. Conversely, the market price for our common stock increased by more than 55% during one trading day in January 2014, in the absence of any news release by us or rumors of which we were aware. The market price of our common stock may fluctuate significantly in response to a number of factors, including:

- the level of our financial resources;
- announcements of entry into or consummation of a financing or strategic transaction;
- changes in the regulatory status of our product candidates, including results of any clinical studies and other research and development programs;
- delays in the completion of our clinical studies or termination of a clinical study, including due to difficulties with patient enrollment or safety issues or inability to produce sufficient quantities of clinical trial material;
- FDA or international regulatory actions and regulatory developments in the U.S. and foreign countries;
- announcements of new products or technologies, commercial relationships or other events (including clinical study results and regulatory events and actions) by us or our competitors;
- announcements of difficulties or delays in commercial manufacture or supply of our drug products;
- market conditions in the pharmaceutical, biopharmaceutical, specialty pharmaceutical and biotechnology sectors;
- developments concerning intellectual property rights generally or those of us or our competitors;
- changes in securities analysts' estimates of our financial performance or deviations in our business and the trading price of our common stock from the estimates of securities analysts;
- events affecting any future collaborations, commercial agreements and grants;
- fluctuations in stock market prices and trading volumes of similar companies;
- sales of large blocks of our common stock, including sales by significant stockholders, our executive officers or our directors or pursuant to shelf or resale registration statements that register shares of our common stock that may be sold by us or certain of our current or future stockholders;
- discussion of us or our stock price by the financial and scientific press and in online investor communities;

- commencement of delisting proceedings by the NYSE MKT;
- additions or departures of key personnel; and
- changes in third-party payor coverage or reimbursement policies.

As evidenced by the February 2016 decline, the realization of any of the foregoing could have a dramatic and adverse impact on the market price of our common stock. In addition, class action litigation has often been instituted against companies whose securities have experienced a substantial decline in market price. Moreover, regulatory entities often undertake investigations of investor transactions in securities that experience volatility following an announcement of a significant event or condition. Any such litigation brought against us or any such investigation involving our investors could result in substantial costs and a diversion of management's attention and resources, which could hurt our business, operating results and financial condition.

Our stock price could decline significantly based on progress with and results of our clinical studies and regulatory agency decisions affecting development of our product candidates.

We expect announcements of progress with and results of clinical studies of our product candidates and regulatory decisions (by us, the FDA, or another regulatory agency) to affect our stock price. Stock prices of companies in our industry have declined significantly when such results and decisions were unfavorable or perceived to be negative or discouraging or when a product candidate did not otherwise meet expectations. If progress in clinical studies or study results are not viewed favorably by us or third parties, including investors, analysts, potential collaborators, the academic and medical communities and regulators, our stock price could decline significantly and you could lose your investment in our common stock.

We may report top-line clinical and nonclinical study data from time to time, which is based on preliminary analysis of then-available data. Such preliminary findings and conclusions are subject to change following a more comprehensive review of the study data. In addition, results of clinical and nonclinical studies often are subject to different interpretations. We may interpret or weigh the importance of study data differently than third parties, including those noted above. Others may not accept or agree with our analysis of study data, which could impact the approvability of our product candidates and/or the value of our development programs and our company in general.

Sales of substantial amounts of our common stock or the perception that such sales may occur could cause the market price of our common stock to decline significantly, even if our business is performing well.

The market price of our common stock could decline as a result of sales by, or the perceived possibility of sales by, us or our existing stockholders of shares of our common stock. Sales by our existing stockholders might also make it more difficult for us to sell equity securities at a time and price that we deem appropriate. Under our existing ATM program, as of June 30, 2016, we may sell up to approximately $23.3 million of additional shares of our common stock. The shelf registration statement on Form S-3 under which the ATM program is registered may be used to register the sale and issuance of more than $99 million of additional securities, subject to limitations if our public float is less than $75 million. In addition, as of August 5, 2016, we have outstanding warrants to purchase approximately 105.2 million additional shares of our common stock. Warrants to purchase more than 13 million of those shares have an exercise price of $0.01 per share and warrants to purchase all but 10.6 million of those shares have an exercise price of less than $1.00 per share. Collectively, the ATM program, the shelf registration statement and the outstanding, in-the-money warrants, may increase the likelihood of sales of substantial amounts of our shares, or the perception that substantial sales may occur, by us or our existing securityholders from time to time, which could cause the market price of our common stock to decline significantly.

We have voting control over shares held by the former principal stockholders of SynthRx and Aires Pharmaceuticals and we will have voting control over shares issuable to former SynthRx stockholders in the future, and we may determine to cause those shares to be voted in such a manner that does not necessarily coincide with the interests of individual stockholders or particular groups of stockholders.

We have voting control with respect to approximately 1.8% of our outstanding common stock (based on shares outstanding as of August 5, 2016), pursuant to agreements we entered into with the former principal stockholders of each of SynthRx and Aires Pharmaceuticals in connection with our acquisition of those companies. Pursuant to the voting and transfer restriction agreement between us and each of the former principal stockholders of SynthRx, we have an irrevocable proxy to vote the shares of our common stock beneficially owned by those stockholders with respect to every action or approval by written consent of our stockholders in such manner as directed by us, except in limited circumstances. If the development of vepoloxamer achieves the remaining milestones set forth in our merger agreement with SynthRx, we will issue an additional 12,478,050 shares of our common stock to the former stockholders of SynthRx and the amount of those shares held by the stockholder parties to the voting and transfer restriction agreement will also be subject to the irrevocable proxy held by us. In addition, pursuant to the stockholder agreements between us and the former principal stockholders of Aires, we have an irrevocable proxy to vote the shares of our common stock issued to such stockholders as merger consideration and then held by such stockholders with respect to every action or approval by written consent of our stockholders in such manner as directed by us, except in limited circumstances, until August 27, 2016. Accordingly, pursuant to

our agreements with the former principal stockholders of SynthRx and Aires, assuming achievement of the remaining milestones under our merger agreement with SynthRx and issuance of all 12,478,050 milestone shares, based on 211,815,450 shares of our common stock outstanding as of August 5, 2016, we would have voting control with respect to approximately 7.4% of our outstanding common stock. As a result, in the future, we may have significant control over substantially all matters requiring approval by our stockholders, including the election of directors and the approval of certain mergers and other business combination transactions. Even if less than all potential milestone-related and holdback shares are issued, our ability to control a potentially significant block of stockholder votes pursuant to these voting agreements may enable us to substantially affect the outcome of proposals brought before our stockholders. Although our board of directors acts in a manner it believes is in the best interest of our stockholders as a whole, the interests of our stockholders as a whole may not always coincide with the interests of individual stockholders or particular groups of stockholders.

Anti-takeover provisions in our charter documents and under Delaware law may make an acquisition of us, which may be beneficial to our stockholders, more difficult, which could depress our stock price.

We are incorporated in Delaware. Certain anti-takeover provisions of Delaware law and our charter documents as currently in effect may make a change in control of our company more difficult, even if a change in control would be beneficial to our stockholders. Our bylaws limit who may call a special meeting of stockholders and establish advance notice requirements for nomination of individuals for election to our board of directors or for proposing matters that can be acted upon at stockholders' meetings. Delaware law also prohibits corporations from engaging in a business combination with any holders of 15% or more of their capital stock until the holder has held the stock for three years unless, among other possibilities, the board of directors approves the transaction. Our board of directors may use these provisions to prevent changes in the management and control of our company. Also, under applicable Delaware law, our board of directors may adopt additional anti-takeover measures in the future. In addition, provisions of certain compensatory contracts with our management, such as equity award agreements, may have an anti-takeover effect by resulting in accelerated vesting of outstanding equity securities held by our executive officers.

Because we do not expect to pay dividends with respect to our common stock in the foreseeable future, you must rely on stock appreciation for any return on your investment.

We have paid no cash dividends on any of our common stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, with respect to our common stock, we do not expect to pay any cash dividends in the foreseeable future, and payment of cash dividends, if any, will also depend on our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our board of directors. Furthermore, we are subject to various laws and regulations that may restrict our ability to pay dividends and we may in the future become subject to contractual restrictions on, or prohibitions against, the payment of dividends. Currently, our debt facility with Hercules prohibits us from declaring and paying any cash dividend on any class of stock or other equity interest. Due to our intent to retain any future earnings rather than pay cash dividends on our common stock and applicable laws, regulations and contractual obligations that may restrict our ability to pay dividends on our common stock, the success of your investment in our common stock will likely depend entirely upon any future appreciation and our common stock may not appreciate.

If we were to issue shares of our common stock or preferred stock that are available for issuance, our stock price could decline.

We have 500,000,000 shares of authorized common stock and, as of August 5, 2016, approximately 126 million of such authorized shares were not outstanding or reserved for issuance under outstanding warrants, options, equity incentive plans or other rights. Subject to applicable securities laws and stock exchange listing requirements, our board of directors is authorized under our charter documents to sell and issue our authorized, but unissued, common stock without stockholder approval and may do so to satisfy our capital requirements or finance the expansion of our product pipeline. Our board of directors also is authorized to issue and sell up to 1,000,000 shares of preferred stock without stockholder approval, at a purchase price approved by the board. The preferred stock may have rights that are superior to the rights of the holders of our common stock. The sale or the proposed sale of substantial amounts of our common stock, preferred stock and/or securities convertible into shares of our common or preferred stock in the public markets may adversely affect the market price of our common stock. Our stockholders may also experience substantial dilution.

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

None.

Item 3. Defaults Upon Senior Securities

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

None.

Item 6. Exhibits

An Exhibit Index has been attached as part of this report and 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.

Mast Therapeutics, Inc.

Date: August 9, 2016

By: /s/ Brian M. Culley
Brian M. Culley
Chief Executive Officer
(Principal Executive Officer)

Date: August 9, 2016

By: /s/ Brandi L. Roberts
Brandi L. Roberts
Chief Financial Officer and Senior Vice President
(Principal Financial and Accounting Officer)

EXHIBIT INDEX

Exhibit No.	Description	Filed Herewith	Incorporated by Reference		
			Form	File/Film No.	Date Filed
10.1#	2016 Executive Incentive Plan		Form 8-K	001-32157-161555255	04/05/16
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a)	X			
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a)	X			
32.1±	Certification of principal executive officer and principal financial officer pursuant to 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	X			
101.INS	XBRL Instance Document	X			
101.SCH	XBRL Taxonomy Extension Schema Document	X			
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	X			
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	X			

# Indicates management contract or compensatory plan

± These certifications are being furnished solely to accompany this report pursuant to 18 U.S.C. 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of the registrant, whether made before or after the date hereof, regardless of any general incorporation by reference language in such filing.

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER PURSUANT TO SECURITIES EXCHANGE ACT RULES 13a-14(a) AND 15(d)-14(a) AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Brian M. Culley, certify that:

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

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

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

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

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

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of 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.

August 9, 2016

/s/ Brian M. Culley
Brian M. Culley
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER PURSUANT TO SECURITIES EXCHANGE ACT RULES 13a-14(a) AND 15(d)-14(a) AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Brandi L. Roberts, certify that:

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

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

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

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

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

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of 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.

August 9, 2016

/s/ Brandi L. Roberts
Brandi L. Roberts
Chief Financial Officer and Senior Vice President
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER 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 of Mast Therapeutics, Inc. (the "Company") on Form 10-Q for the quarter ended June 30, 2016, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Brian M. Culley, principal executive officer of the Company, certify pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

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

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

August 9, 2016

/s/ Brian M. Culley
Brian M. Culley
Chief Executive Officer
(Principal Executive Officer)

In connection with the Quarterly Report of Mast Therapeutics, Inc. (the "Company") on Form 10-Q for the quarter ended June 30, 2016, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Brandi L. Roberts, principal financial officer of the Company, certify pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of her knowledge:

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

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

August 9, 2016

/s/ Brandi L. Roberts
Brandi L. Roberts
Chief Financial Officer and Senior Vice President
(Principal Financial and Accounting Officer)