Mast Therapeutics, Inc.
Form 10-Q
August 12, 2015

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-Q

(Mark One)

x QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the quarterly period ended June 30, 2015

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ¨ No x

The number of shares outstanding of the registrant's common stock, $0.001 par value per share, as of August 10, 2015 was 163,614,297.

TABLE OF CONTENTS

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, 2015	December 31, 2014
Assets		
Current assets:		
Cash and cash equivalents	$21,214	$35,808
Investment securities	22,165	21,481
Prepaid expenses and other current assets	1,374	1,114
Total current assets	44,753	58,403
Property and equipment, net	230	188
In-process research and development	8,549	8,549
Goodwill	3,007	3,007
Other assets	225	353
Total assets	$56,764	$70,500
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$2,005	$1,370
Accrued liabilities	7,845	5,625
Accrued compensation and payroll taxes	950	1,443
Total current liabilities	10,800	8,438
Long-term lease obligation	25	-
Deferred income tax liability	3,404	3,404
Total liabilities	14,229	11,842
Stockholders' equity:		
Common stock, $0.001 par value; 500,000,000 shares authorized; 163,614,297 and 159,458,376 shares issued and outstanding at June 30, 2015 and December 31, 2014, respectively	164	159
Additional paid-in capital	297,260	293,655
Accumulated other comprehensive loss	9	(25)
Accumulated deficit	(254,898)	(235,131)
Total stockholders' equity	42,535	58,658

Total liabilities and stockholders' equity	$56,764	$70,500

See accompanying notes to unaudited condensed consolidated financial statements.

(1)

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,	
	2015	2014	2015	2014
Revenues	$—	$—	$—	$—
Operating expenses:				
Research and development	7,734	4,820	13,776	9,101
Selling, general and administrative	2,410	2,370	5,988	4,636
Transaction-related expenses	-	(11)	-	269
Depreciation and amortization	37	23	67	35
Total operating expenses	10,181	7,202	19,831	14,041
Loss from operations	(10,181)	(7,202)	(19,831)	(14,041)
Interest income	32	17	62	32
Interest expense	(1)	-	(1)	-
Other (expense)/income, net	(1)	33	3	486
Net loss	$(10,151)	$(7,152)	$(19,767)	$(13,523)
Net loss per share - basic and diluted	$(0.06)	$(0.06)	$(0.12)	$(0.12)
Weighted average shares outstanding - basic and diluted	162,128,100	115,587,056	160,800,809	110,349,506
Comprehensive Income/(Loss):				
Net loss	$(10,151)	$(7,152)	$(19,767)	$(13,523)
Other comprehensive income	12	8	35	3
Comprehensive net loss	$(10,139)	$(7,144)	$(19,732)	$(13,520)

See accompanying notes to unaudited condensed consolidated financial statements.

(2)

Mast Therapeutics, Inc. and Subsidiaries

Condensed Consolidated Statements of Cash Flows

(Unaudited)

(in thousands)

	Six Months Ended June 30,	
	2015	2014
Cash flows from operating activities:		
Net loss	$(19,767)	$(13,523)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	67	35
Gain on bargain purchase	—	(486)
Share-based compensation expense	1,578	824
Changes in assets and liabilities, net of effect of acquisitions:		
(Increase)/decrease in prepaid expenses and other assets	(124)	89
Increase/(decrease) in accounts payable and accrued liabilities	2,364	(201)
Net cash used in operating activities	(15,882)	(13,262)
Cash flows from investing activities:		
Purchases of certificates of deposit	(7,986)	(7,981)
Proceeds from maturities of certificates of deposit	7,337	6,626
Purchases of property and equipment	(91)	(109)
Cash obtained through acquisition	—	3,534
Net cash (used in)/provided by investing activities	(740)	2,070
Cash flows from financing activities:		
Proceeds from sale of common stock	2,140	12,474
Payments for capital lease	(3)	—
Payments for offering costs	(109)	(595)
Net cash provided by financing activities	2,028	11,879
Net (decrease)/increase in cash and cash equivalents	(14,594)	687
Cash and cash equivalents at beginning of period	35,808	25,681
Cash and cash equivalents at end of period	$21,214	$26,368

See accompanying notes to unaudited condensed consolidated financial statements.

Mast Therapeutics, Inc. and Subsidiaries

Notes to Condensed Consolidated Financial Statements (Unaudited)

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, 2014, filed with the SEC on March 24, 2015 ("2014 Annual Report"). The condensed consolidated balance sheet as of December 31, 2014 included in this report has been derived from the audited consolidated financial statements included in the 2014 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 clinical-stage, biopharmaceutical company focused on developing 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 nebulizer, which we are developing for the treatment of heart failure with preserved ejection fraction (HFpEF).

Our business, operating results, financial condition, and growth prospects are subject to significant risks and uncertainties, including failing to obtain regulatory approval to commercialize our product candidates and failing to secure additional funding to complete development of and to successfully commercialize our product candidates.

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, 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. Acquisition of Aires

On February 27, 2014, we completed the acquisition of Aires in an all-stock transaction pursuant to the terms of an agreement and plan of merger, dated February 7, 2014, by and among us, AP Acquisition Sub, Inc., a wholly-owned subsidiary of ours, Aires, and a stockholders' representative (the "Merger Agreement"). Aires was a clinical-stage company with its lead product candidate, AIR001 (sodium nitrite) inhalation solution, in Phase 2 studies in pulmonary hypertension. Aires survived the merger transaction as a wholly-owned subsidiary of ours.

Upon completion of the merger, we issued an aggregate of 1,049,706 unregistered shares of our common stock to former Aires stockholders and, in September 2014 after the six-month "holdback" period, we issued an aggregate of 4,053,996 additional unregistered shares of our common stock to former Aires stockholders, all in accordance with the merger agreement. There are no milestone or earn-out payments under the merger agreement; therefore, the total merger consideration was 5,103,702 shares.

We accounted for the acquisition of Aires in accordance with Accounting Standards Codification ("ASC") Topic 805, Business Combinations ("ASC Topic 805"). The total purchase price of the acquisition was approximately $3.3 million. We calculated the purchase price by first multiplying the total number of shares of our common stock issued by $0.80, which was the closing price per share of our common stock on February 27, 2014, the acquisition date. Then, we applied a discount factor to account for lack of market liquidity due to the restrictions on transfer of the securities for a period of six months following the

acquisition in accordance with stockholder agreements we entered into with the former Aires stockholders and the fact that the shares are unregistered and we have no obligation to register them for resale.

Under the acquisition method of accounting, the total purchase price is allocated to Aires' net tangible and intangible assets and liabilities based on their estimated fair values as of the acquisition date. The table below summarizes the estimated fair values of Aires' net tangible and intangible assets and liabilities on the acquisition date (in thousands):

Cash and cash equivalents	$3,534
Prepaid expenses and other assets	86
In-process research and development	2,000
Total assets:	5,620
Accounts payable and accrued liabilities	1,069
Deferred tax liability	795
Total liabilities:	1,864
Net assets acquired	$3,756

The estimated fair value of the net assets acquired exceeds the purchase price by approximately $0.5 million. Accordingly, we recognized the $0.5 million excess as a bargain purchase gain in other (expense)/income net in our condensed consolidated statements of operations and comprehensive loss. We were able to realize a gain because Aires was in a distressed sale situation. Aires lacked sufficient capital to continue operations and was unable to secure additional capital in the timeframe it required.

Acquired In-Process Research and Development

Acquired IPR&D is the estimated fair value of the AIR001 program as of the acquisition date. We determined that the estimated fair value of the AIR001 program was $2.0 million as of the acquisition date 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 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.

To calculate fair value of the AIR001 program under the MPEEM, we used probability-weighted, projected cash flows discounted at a rate considered appropriate given the significant inherent risks associated with drug development by clinical-stage companies. Cash flows were calculated based on estimated projections of revenues and expenses related to AIR001 and then reduced by a contributory charge on requisite assets employed. Contributory assets included debt-free working capital, net fixed assets and assembled workforce. Rates of return on the contributory assets were based on rates used for comparable market participants. Cash flows were assumed to extend through a seven-year market exclusivity period. The resultant cash flows were then discounted to present value using a weighted-average cost of capital for companies with profiles substantially similar to that of Aires, which we believe represents the rate that market participants would use to value the assets. We compensated for the phase of development of the program by applying a probability factor to our estimation of the expected future cash flows. The projected cash flows were based on significant assumptions, including the indication in which we will pursue development of AIR001, the time and resources needed to complete the development and regulatory approval of AIR001, estimates of revenue and operating profit related to the program considering its stage of development, the life of the potential commercialized product, market penetration and competition, and risks associated with achieving commercialization, including delay or failure to obtain regulatory approvals to conduct clinical studies, failure of

clinical studies, delay or failure to obtain required market clearances, and intellectual property litigation.

Deferred Income Tax Liability

The $0.8 million recorded as deferred income tax liability resulting from the acquisition reflects the tax impact of the difference between the book basis and tax basis of acquired IPR&D. Such deferred income tax liability cannot be used to offset deferred tax assets when analyzing our valuation allowance as the acquired IPR&D is considered to have an indefinite life until we complete or abandon development of AIR001.

(5)

4. Goodwill and IPR&D

At June 30, 2015 and December 31, 2014, 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 for our goodwill and our acquired IPR&D related to the SynthRx acquisition as of September 30, 2014 and a quantitative assessment for our acquired IPR&D related to the Aires acquisition as of February 27, 2015. No impairment was noted.

5. 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, including those with maturities beyond one year from the date of purchase, 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, 2015, $5.6 million, or approximately 25%, of our investment securities had contractual maturity dates of more than one year and less than or equal to 18 months and none were greater than 18 months.

At June 30, 2015 and December 31, 2014, our investment securities were as follows (in thousands):

	June 30, 2015	December 31, 2014
Fair value of investment securities	$22,165	$ 21,481
Cost basis of investment securities	22,156	21,506

	June 30, 2015	December 31, 2014
Net unrealized gains/(losses) on investment securities	9	(25)

6. 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, 2015 and December 31, 2014 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, 2015:				
Cash equivalents	$16,529	$16,529	$—	$ —
Investment securities	$22,165	$—	$22,165	$ —
At December 31, 2014:				
Cash equivalents	$16,626	$16,626	$—	$ —
Investment securities	$21,481	$—	$21,481	$ —

7. 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 phone equipment under a lease agreement classified as a capital lease. The lease obligation is $35,000 with an interest rate of 7.94% per annum and the lease expires in December 2019. The equipment is being amortized over five years.

8. Accrued Liabilities

Accrued liabilities at June 30, 2015 and December 31, 2014 were as follows (in thousands):

	June 30, 2015	December 31, 2014
Accrued R&D agreements and study expenses	$7,409	$ 5,383
Other accrued liabilities	436	242
Total accrued liabilities	$7,845	$ 5,625

(7)

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, 2015 and 2014 was as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2015	2014	2015	2014
Selling, general and administrative expense	$371	$347	$1,312	$688
Research and development expense	141	77	266	136
Share-based compensation expense	$512	$424	$1,578	$824

During the six months ended June 30, 2015, 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, 2014	13,616,137	$ 1.00
Granted	12,517,702	$ 0.55
Exercised	—	$ —
Expired/forfeited	(3,678,570)	$ 0.59
Outstanding at June 30, 2015	22,455,269	$ 0.82

At June 30, 2015, total unrecognized estimated compensation cost related to non-vested employee and non-employee director share-based awards granted prior to that date was $5.2 million, which is expected to be recognized over a weighted-average period of 3.2 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, 2015 and 2014 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,	
	2015	2014	2015	2014
Options	20,148,555	10,103,538	20,454,379	9,760,100
Warrants	76,559,927	44,547,678	77,847,594	44,566,699

11. Recent Accounting Pronouncements

In August 2014, the FASB issued Accounting Standards Update (“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, 2015 and 2014 are as follows (in thousands):

	Six Months Ended June 30,	
	2015	2014
Supplemental disclosures of non-cash investing and financing activities:		
Issuance of common stock for acquisitions	$-	$3,270
Assumptions of liabilities in acquisitions	$-	$1,069
Unrealized gain on investment securities	$(35)	$(3)
Purchases of property and equipment in accounts payable	$-	$2
Financing costs in accounts payable and accrued liabilities	$-	$41

13. Stockholders' Equity

Underwritten Public Offering of Common Stock, Pre-funded Warrants and Warrants

In November 2014, we completed an underwritten public offering of 30,941,102 shares of our common stock, 13,081,428 "pre-funded" warrants exercisable for up to 13,081,428 shares of our common stock, and 22,011,265 warrants exercisable for up to 22,011,265 shares of our common stock. These securities were offered and sold to the underwriters and the public in units with each Series A unit consisting of one share of our common stock and one-half (0.5) of a warrant and each Series B unit consisting of one pre-funded warrant and one-half (0.5) of a warrant. Each whole warrant is exercisable for one share of our common stock. We sold an aggregate of 30,941,102 Series A units and 13,081,428 Series B units. The gross proceeds from this financing were $21.0 million and, after deducting underwriting discounts and commissions and other offering expenses, our net proceeds were $19.7 million. We may receive up to $0.1 million and $16.5 million of additional proceeds from the exercise of the pre-funded warrants and warrants, respectively, issued in the offering. The exercise price of the pre-funded warrants is $0.01 per share and exercise price of the warrants is $0.75 per share. Subject to certain beneficial ownership limitations, the pre-funded warrants and warrants are exercisable at any time on or before November 12, 2019.

"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 million, from time to time, through an "at the market" equity offering program (the "ATM program"), under which Cowen acts as sales agent. As of June 30, 2015, we had sold and issued an aggregate of 24,859,107 shares at a weighted-average sales price of $0.70 per share under the ATM program for aggregate gross proceeds of $17.5 million and $16.6 million in net proceeds, after deducting sales agent

commission and discounts and our other offering costs.

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.

(9)

Outstanding Warrants

At June 30, 2015, outstanding warrants to purchase shares of common stock are as follows:

Shares Underlying Outstanding Warrants	Exercise Price	Expiration Date
2,046,139	$ 2.750	January 2016
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
75,861,232		

14. Subsequent Events

Loan and Security Agreement

In August 2015, we entered into a loan and security agreement ("the Loan Agreement") with Hercules Technology III, L.P. and Hercules Technology Growth Capital, Inc. (together, "Hercules") under which we may borrow up to $15.0 million in two tranches. We borrowed the first tranche ("Tranche 1") of $5.0 million upon entry into the Loan Agreement on August 11, 2015 and paid a facility charge of $75,000. We previously paid a commitment charge of $25,000. We plan to use the proceeds from Tranche 1 to provide additional funding for our development programs and for general corporate purposes.

The other tranche of $10.0 million ("Tranche 2") is available through December 31, 2015, provided that our vepoloxamer and AIR001 programs achieve certain clinical development milestones and we receive net cash proceeds of at least $15.0 million from either, or a combination of, upfront cash payments from one or more strategic corporate partnerships or one or more equity financings.

The interest rate for any outstanding amounts 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 are interest only until June 1, 2016, followed by 30 equal monthly payments of principal and interest. In addition, a final payment of up to $712,500 will be due on the scheduled maturity date of January 1, 2019. Interest only payments may be extended through March 1, 2017 based upon the achievement of a clinical development milestone as well as the draw of Tranche 2, which would extend our maturity date out to October 1, 2019. If we elect to prepay the outstanding amount 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. Our obligations under the Loan Agreement are secured by a 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.

Issuance of Warrant

In connection with the Loan Agreement, on August 11, 2015, we entered into a Warrant Agreement with and issued a warrant to Hercules Technology III, L.P. evidencing the right to purchase shares of our common stock at an exercise price of $0.41 per share (the "Warrant"). The Warrant initially is exercisable for 853,658 shares of our common stock. If we elect to draw Tranche 2, then on the date we receive the additional advance, the Warrant automatically will become exercisable for an additional 426,829 shares. The exercise price and the number of shares underlying the Warrant are subject to adjustment in the event of a merger event, reclassification of our common stock, subdivision or combination of our common stock, or certain dividend payments. The Warrant is exercisable until August 11, 2020. 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.

(10)

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, 2014, filed with the U.S. Securities and Exchange Commission, or SEC, on March 24, 2015, 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., 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 clinical-stage, biopharmaceutical company developing novel therapies for serious or life-threatening diseases with significant unmet needs. 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 (also known as MST-188), our lead drug candidate. Vepoloxamer 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. We currently are developing vepoloxamer for the treatment of sickle cell disease, heart failure, and stroke. We also are developing AIR001, a sodium nitrite solution for intermittent inhalation via nebulizer. AIR001 has demonstrated positive hemodynamic effects in patients with pulmonary hypertension and we are developing it for the treatment of heart failure with preserved ejection fraction, or 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 $19.8 million for the six months ended June 30, 2015. As of June 30, 2015, we had an accumulated deficit of $254.9 million. Our cash, cash equivalents, and investment securities were $43.4 million as of June 30, 2015.

We continue to focus our resources primarily on the development of vepoloxamer. Enrolling subjects in EPIC, our pivotal Phase 3 study of vepoloxamer in patients with sickle cell disease, is one of our top priorities. We also plan to initiate a Phase 2 study of vepoloxamer in patients with chronic heart failure in the third quarter of 2015. In addition, based on a growing body of nonclinical data we and others have generated, and following recent meetings with medical experts in the field, we have determined to initiate a clinical development program in stroke. Previously, we planned to first demonstrate the potential utility of vepoloxamer in acute thrombotic arterial diseases with a clinical study in acute limb ischemia, or ALI, and leverage the ALI study data to support a clinical development plan in stroke. However, based on nonclinical data we announced earlier this year, as well as published data from recent institutional studies of poloxamer 188, we believe, and medical experts in the field have agreed, that sufficient data now exists to support clinical development of vepoloxamer in stroke, and we have determined to commence a clinical program in stroke and discontinue our clinical program in ALI. Accordingly, we are taking steps to wind down our Phase 2 study in ALI. Our vepoloxamer pipeline also includes a preclinical development program in resuscitation following major trauma (i.e., restoration of circulating blood volume and pressure).

Our second product candidate, AIR001, is being tested in multiple institution-sponsored Phase 2a clinical studies in patients with HFpEF. We obtained the AIR001 program through our acquisition of Aires Pharmaceuticals, Inc. in February 2014. Prior to the acquisition, AIR001 had been tested in more than 120 healthy volunteers and patients with various forms of pulmonary hypertension and it demonstrated positive hemodynamic effects and was well-tolerated. If data from the Phase 2a studies are positive, we expect to conduct a Phase 2b proof-of-concept study in HFpEF.

Acquisition of Aires Pharmaceuticals

In February 2014, we acquired Aires Pharmaceuticals, Inc. in a merger transaction, which resulted in Aires becoming our wholly-owned subsidiary. Upon completion of the merger, we issued an aggregate of 1,049,706 unregistered shares of our common stock to former Aires stockholders and, in September 2014, following a six-month “holdback” period, we issued an aggregate of 4,053,996 additional unregistered shares of our common stock to former Aires stockholders, all in accordance with the merger agreement. There are no milestone or earn-out payments under the merger agreement. Accordingly, the total merger consideration was 5,103,702 shares.

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 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, and quality assurance and regulatory affairs services. 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 and related consulting fees. 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 new drug application, or 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.

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 market research functions, and professional and consulting fees for accounting, legal, investor relations, business development, market research, human resources and information technology services. Other SG&A expenses include facility lease and insurance costs.

Transaction-Related Expenses. Transaction-related expenses consist of legal, accounting, financial and business development advisory fees associated with the evaluation of potential acquisition targets and execution of acquisition transactions, including our acquisitions of Aires and SynthRx.

Other Income, Net. Other income, net includes the bargain purchase gain related to the acquisition of Aires in 2014, as well as unrealized and realized gains and losses from foreign currency transactions and other non-operating gains and losses.

Comparison of Three Months Ended June 30, 2015 and 2014

Revenue. We recognized no revenue for the three months ended June 30, 2015 and 2014.

R&D Expenses. Our R&D expenses for the three months ended June 30, 2015 consisted primarily of external costs associated with the EPIC study and research-related manufacturing for vepoloxamer and AIR001. These expenses consisted primarily of CRO and CMO expenses, clinical study-related consulting 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,					
	2015	%		2014	%	
External clinical study fees and expenses	$3,703	48	%	$2,898	60	%
External nonclinical study fees and expenses	2,877	37	%	1,009	21	%
Personnel costs	1,013	13	%	836	17	%
Share-based compensation expense	141	2	%	77	2	%
Total	$7,734	100	%	$4,820	100	%

R&D expenses increased by $2.9 million, or approximately 60.5%, to $7.7 million for the three months ended June 30, 2015, compared to $4.8 million for the same period in 2014. This increase was due primarily to a $1.9 million increase in external nonclinical study fees and expenses, a $0.8 million increase in external clinical study fees and expenses and a $0.2 million increase in personnel expenses.

The $1.9 million increase in external nonclinical study fees and expenses was due primarily to a $1.7 million increase in research-related manufacturing costs for vepoloxamer and a $0.2 million increase in research-related manufacturing costs for AIR001. The $0.8 million increase in external clinical study fees and expenses was due primarily to an increase of $1.2 million in EPIC study costs, offset by a decrease of $0.4 million in AIR001 study costs.

SG&A Expenses. SG&A expenses of $2.4 million for the three months ended June 30, 2015 were consistent with the same period in 2014.

Transaction-Related Expenses. There were no transaction-related expenses for the three months ended June 30, 2015. Transaction-related expenses for the three months ended June 30, 2014 were negligible.

Other (Expense)/Income, Net. Other (expense)/income, net for the three months ended June 30, 2015 was negligible. Other (expense)/ income, net for the three months ended June 30, 2014 consisted primarily of a $33,000 adjustment to the bargain purchase gain associated with the acquisition of Aires.

Net Loss. Net loss was $10.2 million, or $0.06 per share, for the three months ended June 30, 2015, compared to net loss of $7.2 million, or $0.06 per share, for the same period in 2014.

Comparison of Six Months Ended June 30, 2015 and 2014

Revenue. We recognized no revenue for the six months ended June 30, 2015 and 2014.

R&D Expenses. Our R&D expenses for the six months ended June 30, 2015 consisted primarily of external costs associated with the EPIC study, our Phase 2 study of vepoloxamer in ALI, and research-related manufacturing for vepoloxamer and AIR001. These expenses consisted primarily of CRO and CMO expenses, clinical study-related consulting 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,					
	2015	%		2014	%	
External clinical study fees and expenses	$7,210	52	%	$5,229	57	%
External nonclinical study fees and expenses	4,393	32	%	2,096	23	%
Personnel costs	1,907	14	%	1,640	18	%
Share-based compensation expense	266	2	%	136	2	%
Total	$13,776	100	%	$9,101	100	%

R&D expenses increased by $4.7 million, or approximately 51.4%, to $13.8 million for the six months ended June 30, 2015, compared to $9.1 million for the same period in 2014. This increase was due primarily to a $2.3 million increase in external nonclinical study fees and expenses, a $2.0 million increase in external clinical study fees and expenses and a $0.3 million increase in personnel expenses.

The $2.3 million increase in external nonclinical study fees and expenses was due primarily to a $2.0 million increase in research-related manufacturing costs for vepoloxamer and a $0.3 million increase in research-related manufacturing costs for AIR001. The $2.0 million increase in external clinical study fees and expenses was due primarily to an increase of $2.5 million in EPIC study costs, offset by a decrease of $0.5 million in AIR001 study costs.

SG&A Expenses. SG&A expenses increased by $1.4 million, or approximately 29.2%, to $6.0 million for the six months ended June 30, 2015, compared to $4.6 million for the same period in 2014. This increase was due primarily to a $0.8 million increase in personnel costs and a $0.3 million increase in professional and consulting fees. Personnel costs for the six months ended June 30, 2015 include $0.4 million of severance expense 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.

Transaction-Related Expenses. There were no transaction-related expenses for the six months ended June 30, 2015. Transaction-related expenses of $0.3 million for the six months ended June 30, 2014 consisted primarily of legal fees associated with the acquisition of Aires.

Other (Expense)/Income, Net. Other (expense)/income, net for the six months ended June 30, 2015 was negligible. Other (expense)/income, net for the six months ended June 30, 2014 consisted primarily of a $0.5 million bargain purchase gain associated with the acquisition of Aires.

Net Loss. Net loss was $19.8 million, or $0.12 per share, for the six months ended June 30, 2015, compared to net loss of $13.5 million, or $0.12 per share, for the same period in 2014.

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, 2015, we incurred a loss from operations of $19.8 million. Our cash, cash equivalents and investment securities were $43.4 million as of June 30, 2015.

We historically have funded our operations principally through proceeds from sales of our equity securities. In November 2014, we completed an underwritten public offering with gross proceeds of $21.0 million from the sale and issuance of units consisting of shares of our common stock and warrants to purchase our common stock at an exercise price of $0.75 per share and units consisting of "pre-funded" warrants to purchase shares of our common stock at an exercise price of $0.01 per share and warrants to purchase shares of our common stock at an exercise price of $0.75 per share. We issued and sold an aggregate of 30,941,102 shares of our common stock, 13,081,428 pre-funded warrants exercisable for up to 13,081,428 shares, and 22,011,265 warrants exercisable for up to 22,011,265 shares. Net proceeds, after deducting underwriting discounts and commissions and other offering expenses, were $19.7 million. The pre-funded warrants and the warrants are exercisable at any time on or before November 12, 2019, subject to certain beneficial ownership limitations.

We may receive up to $5.6 million, $11.7 million, $18.3 million, $0.1 million and $16.5 million of additional net proceeds from the exercise of warrants issued in the registered direct equity financings we completed in January 2011 and the underwritten public offerings we completed in November 2011, June 2013 and November 2014, respectively. 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 $2.75, $1.10, $0.65, $0.01 and $0.75 per share, respectively. In comparison, the closing sale price of our common stock on June 30, 2015 was $0.49 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 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 million, from time to time, through an "at the market" equity offering program, or ATM program, under which Cowen acts as sales agent. As of June 30, 2015, in the aggregate since we commenced the ATM program, we had sold and issued 24,859,107 shares at a weighted-average sales price of $0.70 per share under the ATM program for aggregate gross proceeds of $17.5 million and $16.6 million in net proceeds, after deducting sales agent commission and discounts and our other offering costs.

In August 2015, we entered into a loan and security agreement with Hercules Technology III, L.P. and Hercules Technology Growth Capital, Inc., together referred to as Hercules, under which we may borrow up to $15.0 million in two tranches. We borrowed the first tranche of $5.0 million upon entry into the agreement with Hercules on August 11, 2015, and received approximately $4.8 million, net of fees. Our ability to borrow the additional $10.0 million under the loan agreement is subject to our achievement of certain clinical development and financial milestones by December 31, 2015, as described in Note 14, "Subsequent Events," of the Notes to the Condensed Consolidated Financial Statements (Unaudited) in Part I, Item 1 of this report. Even if it is available to us under the terms of our agreement with Hercules, we have no obligation to borrow the additional $10.0 million. Our obligations under the Loan Agreement 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 Loan Agreement includes other customary restrictive covenants that may limit our ability to raise capital through other debt or equity financing.

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

Operating activities. 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. Net cash used in operating activities was $13.3 million for the six months ended June 30, 2014 and consisted primarily of a net loss of $13.5 million adjusted for non-cash items, including share-based compensation expenses of $0.8 million, offset by a net decrease of $0.1 million due to changes in assets and liabilities and a gain on bargain purchase of $0.5 million.

Investing activities. Net cash used in investing activities was $0.7 million for the six months ended June 30, 2015 compared to net cash provided by investing activities of $2.1 million for the same period in 2014. In the six months ended June 30, 2014, we obtained $3.5 million of cash through our acquisition of Aires.

Financing activities. Net cash provided by financing activities was $2.0 million for the six months ended June 30, 2015, representing the net proceeds from sales of our shares of common stock through our ATM program, less payments under a capital lease agreement for our phone equipment. Net cash provided by financing activities was $11.9 million for the six months ended June 30, 2014, representing the net proceeds from sales of our shares of common stock through our ATM program.

Management Outlook

We anticipate that our cash, cash equivalents and investment securities as of June 30, 2015, together with the borrowing under our debt facility, will be sufficient to fund our operations for at least the next 12 months. We expect our operating expenses for the last six months of 2015 will be approximately $18 million to $20 million, excluding share-based compensation expense.

Our estimate of our operating expenses for the remaining six months of 2015 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 and 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 operating expenses and future capital requirements include, but are not limited to:

- 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;
- our ability to manage timelines and costs related to commercial manufacture of our products, should any of our product candidates obtain regulatory approval;
- the extent to which we increase our workforce, including in connection with establishing or acquiring sales and distribution capabilities;
- our ability to protect our intellectual property and 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. Enrolling subjects in the EPIC study is one of our top priorities. We expect to enroll 388 subjects into EPIC and we have enrolled more than 70% of those subjects. There are more than 70 EPIC study sites in more than ten countries, including approximately 50 sites in the United States, and we anticipate opening new study sites in up to four additional countries. Although predicting the rate of enrollment and timing of availability of data for any clinical study, including EPIC, is subject to a number of significant assumptions and completion of the study and timing of data may differ materially, we expect to announce top-line results in the first quarter of 2016.

In addition to EPIC, we are conducting other activities to evaluate vepoloxamer’s potential in sickle cell disease, including enrolling patients participating in EPIC at selected U.S. study sites in a sub-study to investigate and quantify

the effect of vepoloxamer on tissue oxygenation using non-invasive methods. Further, during the second quarter of 2015, we initiated an open-label, multicenter extension study called EPIC-E to expand our existing safety database regarding repeat exposure to vepoloxamer. The study will enroll patients who have completed the EPIC study and are hospitalized for subsequent vaso-occlusive crisis. To further enhance the safety database for our new drug application and help guide dosage adjustments for special populations, we also plan to initiate a clinical study of vepoloxamer in approximately 30 patients with varying degrees of renal impairment.

We also are advancing our other vepoloxamer programs. Encouraged by positive results from randomized, placebo-controlled, nonclinical proof-of-concept and repeat-treatment studies of vepoloxamer in a model of advanced heart failure, as well as recommendations from medical experts in the field, we plan to initiate a proof-of-concept Phase 2 study of vepoloxamer in patients with chronic heart failure in the third quarter of 2015. While we are still in the planning process, we expect the study will enroll approximately 150 patients to evaluate the safety and efficacy of a single administration of vepoloxamer compared to placebo, including vepoloxamer's effect on markers of cardiac injury (troponin) and wall stress (NT-proBNP), as well as clinical outcomes. We expect to conduct the study on an outpatient basis at medical centers within and outside of the U.S.

We also are evaluating vepoloxamer's potential in stroke. Based on a growing body of nonclinical data we and others have generated, and following recent meetings with medical experts in the field, we have determined to initiate a clinical development program in stroke. Previously, we planned to first demonstrate the potential utility of vepoloxamer in acute thrombotic arterial diseases with a clinical study in ALI and leverage the ALI study data to support a clinical development plan in stroke. However, based on nonclinical data we announced earlier this year, as well as published data from recent institutional studies of poloxamer 188, we believe, and medical experts in the field have agreed, that sufficient data now exists to support clinical development of vepoloxamer in stroke, and we have determined to commence a clinical program in stroke and discontinue our clinical program in ALI. Accordingly, we are taking steps to wind down our Phase 2 study in ALI. We anticipate the cost savings from discontinuing the ALI study to more than offset 2015 expenses related to pursuing clinical development in stroke.

In addition to our clinical studies, we are conducting or plan to conduct a number of other ex vivo, nonclinical in vivo and in vitro studies of vepoloxamer to further characterize its pharmacologic effects and support our intellectual property positions. We also are conducting and plan to conduct additional research-related manufacturing activities, some of which may result in additional intellectual property rights and protection for our product candidates.

AIR001

Based on the positive hemodynamic effects observed in Phase 1 and Phase 2 studies of AIR001 in more than 120 healthy volunteers and patients with various forms of pulmonary hypertension and data showing AIR001 was well tolerated in those studies, we believe AIR001 may be uniquely suitable to address the serious unmet need of patients with HFpEF. To better understand AIR001's potential in that patient population, we are supporting ongoing Phase 2a studies of AIR001 in patients with HFpEF sponsored by Mayo Clinic and the University of Pittsburgh. We anticipate reporting preliminary data from Mayo Clinic's study in the second half of 2015. Mayo Clinic is enrolling approximately 30 subjects in a randomized, double-blind, placebo-controlled study to evaluate the effects of AIR001 on resting and exercise hemodynamics in patients with HFpEF referred to the cardiac catheterization laboratory for invasive exercise stress testing. Pending results from these Phase 2a studies, we expect to conduct a Phase 2b proof-of-concept study of AIR001 in HFpEF.

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.

Although we anticipate that our cash, cash equivalents and investment securities, including the borrowing under our debt facility, will be sufficient to fund our operations for at least the next 12 months, we do not anticipate that such capital alone will be sufficient to fund our operations through the completion of development and commercialization of our product candidates. In addition, we may utilize our financial resources sooner than we currently expect if we incur unanticipated expenses or we pursue development or commercial-readiness activities for our product candidates at levels or on timelines other than currently planned or we expand our product pipeline through acquisition of new product candidates and/or technologies. For the foreseeable future, we plan to fund our operations through public or private equity and/or debt financings and through collaborations, including licensing arrangements. However, adequate additional capital may not be available to us in the future on acceptable terms, on a timely basis, or at all. Our failure to raise capital as and when needed would have a 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,” “indicat 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, timing of initiation and completion, and costs of clinical studies and nonclinical testing, the indications in which we plan to pursue development of our product candidates, our plans regarding partnering or other collaborative arrangements and for raising additional capital to support our operations, and our belief that we have

sufficient liquidity to fund our operations for at least the next 12 months. 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:

- our ability, or that of a future partner, to successfully develop, obtain regulatory approval for, and then successfully commercialize our product candidates;
- 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 maintain our relationships with the single-source third-party manufacturers and suppliers for clinical trial material, including the API and finished drug product, and the ability of such manufacturers and suppliers to successfully and consistently meet our manufacturing and supply requirements;
- 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;
- our ability to obtain additional capital as needed on acceptable terms, or at all;
- 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 in sickle cell disease prior to accepting a new drug application for review or granting regulatory approval, even if the EPIC study is successful;
- 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 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 establish and protect our intellectual property rights related to our product candidates;
- 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;

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potential product liability exposure and, if successful claims are brought against us, liability for a product or product candidate;

(20)

- 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 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

Under SEC rules and regulations, as a smaller reporting company we are not required to provide the information required by this item.

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, 2015. Based on that evaluation, our principal executive officer and principal financial officer have concluded that as of June 30, 2015 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 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, 2014.

RISKS RELATED TO OUR BUSINESS

Risks Related to Our Capital Requirements, Finances and Operations

We have incurred losses since our inception, we expect our operating expenses to continue to exceed our revenue for the foreseeable future, and we may never generate revenue sufficient to achieve profitability.

We are a clinical-stage 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, 2014, we incurred a loss from operations of $29.3 million and, as of June 30, 2015, we had an accumulated deficit of $254.9 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 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, we enter into an arrangement that provides for licensing revenue or other partnering-related funding or one of our product candidates is approved by the FDA or another regulatory agency and successfully marketed, outcomes which we may not achieve.

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, 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. We are focusing our resources primarily on the development of vepoloxamer. Accordingly, the success of our business 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. 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. 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 process of developing and seeking regulatory approval of 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 and scope of development programs we pursue;
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, 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 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; 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.

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.*

We have a debt facility for up to $15 million with an outstanding principal balance of $5 million with Hercules Technology Growth 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 customary 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. 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. Hercules could declare a default upon the occurrence of any event that it interprets as a material adverse effect as defined under the loan and security agreement, thereby requiring us to repay the loan immediately or renegotiate the terms of the agreement. 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.

We will need to obtain additional funding to pursue our current business strategy 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 dilution to our existing stockholders, require us to relinquish significant rights, or restrict our operations.

We anticipate that our cash, cash equivalents and investment securities as of June 30, 2015, together with the borrowing under our debt facility, will be sufficient to fund our operations for at least the next 12 months. However, we may determine to grow our organization and/or pursue development activities for our product candidates at levels

or on timelines, or we may incur unexpected expenses, that shorten the period through which our current operating funds will sustain us. Additionally, we may seek to further expand our product pipeline through acquisition of additional product candidates and/or technologies and the cost to acquire and develop such new product candidates and/or technologies may shorten the period through which our current operating funds will sustain us. We do not expect to generate any substantial revenue from operations until, and unless, one of our product candidates receives regulatory approval and we commence commercial sales or we enter into an arrangement that provides for licensing revenue or other partnering-related funding.

For the foreseeable future, we likely will seek to fund our operations through public or private equity and debt financings and/or through collaborations, such as licensing arrangements or partnering transactions, and may execute any such transaction at any time,

subject to applicable laws and regulations. Although we were able to raise significant funds in the past through equity financings, 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 any effort 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.

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

Historically, we have raised capital 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 163,614,297 shares of our common stock outstanding as of August 10, 2015 and the closing price per share of our common stock on such date, which was $0.40, we could not raise more than approximately $13.1 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. 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.

If we are unable to raise sufficient additional capital as needed, we may be forced to delay, scale back or discontinue development of our product candidates, partner them 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, scale back or discontinue one or more of our development programs, or to seek collaborators at an earlier stage than otherwise would be desirable or on terms less favorable than might otherwise be available. 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. Delays in and/or reduction of development 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 be 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.

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. Competition for qualified

personnel, particularly for key positions, is intense among companies in our field, universities and other research organizations, particularly in the San Diego, California area, and many of the organizations against which we compete for qualified personnel have greater financial and other resources and different risk profiles than our company, which may make them more attractive employers. Our ability to compete for qualified personnel 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 products 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, 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 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 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 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 significant additional information and there is no guarantee that our product candidate will be approved for the treatment of 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 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, which would 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;
- obtaining institutional review board, or IRB, approval to conduct a clinical study at a prospective site;
- 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;
- 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

(29)

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. 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.

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. For example, if we are unable to maintain our relationship with our current supplier of vepoloxamer, 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 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. 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, we may have insufficient quantities of clinical trial material for our ongoing and/or planned clinical studies, including EPIC. 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. We cannot ensure that manufacturing or quality control problems will not arise in connection with the manufacture of our clinical trial material, or that third-party manufacturers will be able to maintain the necessary governmental licenses and approvals to continue manufacturing such clinical trial material. 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 no clinically significant changes in renal function were observed. However, patient safety concerns 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, we may have limited control over nonclinical testing or clinical studies that may be conducted by such third-party licensees in those territories or indications. 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 and with interpretation of the results of those studies, 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.

The CROs that we engage to execute our clinical studies play a significant role in the conduct of the studies and subsequent collection and analysis of 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 currently is being tested in institution-sponsored clinical studies and, because we are not the study sponsor, our control over these studies is further limited. If CROs and/or 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 or are planning to conduct in parallel with EPIC. 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 approved 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.

We currently have limited marketing capabilities and no sales capability and our failure to acquire or develop these and related capabilities internally or contract with third parties to perform these activities successfully could delay and/or limit our ability to generate revenue in the event we receive regulatory approval to market one of our product candidates.

We currently have limited marketing capabilities and no sales capability and our company has never marketed or sold products. To commercialize our vepoloxamer product candidate or any other product candidate, we will have to acquire or develop marketing, distribution, sales and associated regulatory compliance capabilities, or rely on marketing partners or other third parties for the marketing, distribution and sale of our products. 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. The acquisition or development of commercialization and associated regulatory compliance capabilities likely will require substantial financial and other resources and divert the attention of our management and key personnel, and, if not completed on time, could delay the launch of an approved product, and otherwise negatively impact our product development and commercialization efforts.

To the extent we establish marketing, distribution or sales arrangements with 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 products 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 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 patents and other intellectual property protection we obtain that cover 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;
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
(36)

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, including ours, are uncertain and involve complex legal and factual questions. 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.

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. There can be no assurance, however, that binding agreements will not be breached, that we will have adequate remedies for any breach, or that trade secrets or other proprietary information will not otherwise become known or be independently discovered by competitors. 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.

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 the use of poloxamer 188 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 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 application covering a purportedly novel composition of poloxamer material may be limited to the specific method by which we manufacture the material. Even if claims issue, a competitor may develop a method to manufacture our poloxamer material using a different process, in which case the competitor may not infringe our “product-by-process” claims.

The cost of litigation to uphold the validity and prevent infringement of our patents could be substantial. Furthermore, 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. We can provide no assurance that our 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 we are sued for infringing the proprietary rights of third parties, it will 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 or selling 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. 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 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, acute limb ischemia and other orphan indications we may pursue. Legislative action, such as the Food and Drug Administration Safety and Innovation Act, which was signed into law in 2012, 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. Some of our potential competitors in sickle cell disease 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 compound in adult and pediatric patients with sickle cell disease experiencing vaso-occlusive crisis, and the study likely will compete with EPIC for patients and may adversely affect enrollment in EPIC, which could delay completion of our study. In addition, Eli Lilly and Company is conducting a Phase 3 study of prasugrel in pediatric patients with sickle cell disease to assess whether it reduces the rate of vaso-occlusive crisis. Emmaus Life Sciences, Inc. has announced its plans to submit an NDA to the FDA in 2015 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.

With respect to competition for vepoloxamer for complications of arterial disease, although we intend first to develop vepoloxamer as an adjunct to thrombolytics, it could compete with current revascularization methods, including thrombolytics. In addition, we are aware of a number of potentially competitive investigational therapies for severe forms of thrombotic arterial disease, including angiogenic growth factors, vasoactive drugs, anticoagulants, thrombolytics, anti-platelet agents, cytoprotectives, and blood substitutes, some of which are in late-stage clinical development. Should any of these other investigational therapies receive regulatory approval prior to vepoloxamer, they may become entrenched in the standard of care, diminish the need for vepoloxamer, or be difficult to displace.

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.

Our ability to commercialize our products successfully 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 managed healthcare organizations. These third-party payors are increasingly challenging the prices charged for medical products and services and, if they do not consider our products to be cost-effective compared to other therapies, they may not cover them as a benefit under their plans or, if covered, the level of reimbursement may not be sufficient to allow us to sell our products on a profitable basis. Significant uncertainty exists as to the coverage and

reimbursement status of newly approved drug products, including coding, coverage and payment. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services 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 drugs have been a focus in this effort. Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. Even if reimbursement is provided, market acceptance of our

products would 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. There have been federal and state proposals to subject the pricing of healthcare goods and services to government control and to make other changes to the U.S. healthcare system. 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. For example, we may determine to pursue development or other activities or grow our organization or product pipeline or at levels or on timelines that reduces our stockholders' equity 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, on August 10, 2011, the market price for our common stock dropped almost 60% following our announcement of our receipt of a complete response letter to our NDA for Exelbine, which letter stated that the FDA could not approve Exelbine in its present form. 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 August 10, 2011 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. In February 2014, we commenced a $30 million "at the market" offering program, or ATM program, and, as of June 30, 2015, we had raised gross proceeds of approximately $17.5 million under that program. In March 2015, we filed a new shelf registration statement on Form S-3 to register the sale and issuance of up to an additional $150 million of our securities, subject to limitations if our public float is less than $75 million. In addition, we have outstanding warrants to purchase approximately 75.9 million additional shares of our common stock and warrants to purchase more than 13 million of

those shares have an exercise price of $0.01 per share and warrants to purchase another 50.1 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 3.5% of our outstanding common stock (based on shares outstanding as of August 10, 2015), 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 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 163,614,297 shares of our common stock outstanding as of August 10, 2015, we would have voting control with respect to approximately 10.0% 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. In particular, in the event of a change in control, the vesting of options we granted since July 2009 to our chief executive officer will accelerate with respect to fifty percent of the then unvested shares on the day prior to the date of the change in control and, subject to his continuous service, with respect to the remaining fifty percent of the then unvested shares on the one year anniversary of the date of the change in control, and could accelerate in full at the time of the change in control if the acquirer does not assume or substitute for the options. As a result, if an acquirer desired to retain the services of our chief executive officer following an acquisition, it may be required to provide additional incentive to

him, which could increase the cost of the acquisition to the acquirer and may deter or adversely affect the terms of the potential acquisition.

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 10, 2015, more than 203 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

Loan and Security Agreement

On August 11, 2015, we entered into a loan and security agreement, or the Loan Agreement, with Hercules Technology III, L.P. and Hercules Technology Growth Capital, Inc., together referred to as Hercules, under which we

may borrow up to $15.0 million in two tranches. Upon entry into the Loan Agreement, we borrowed the first tranche of $5.0 million and paid a facility charge of $75,000. We previously paid a commitment charge of $25,000. The other tranche of $10.0 million ("Tranche 2") is available through December 31, 2015, provided that our vepoloxamer and AIR001 programs achieve certain clinical development milestones and we receive unrestricted and unencumbered net cash proceeds of at least $15.0 million from either, or a combination of, upfront cash payments from one or more strategic corporate partnerships or one or more equity financings.

The interest rate for any outstanding amounts 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 are interest only until June 1, 2016 (which may be extended up to March 1, 2017 as specified in the Loan Agreement based upon the achievement of a clinical development milestone as well as our draw of Tranche 2), followed by 30 equal monthly payments of principal and interest. In addition, a final payment of up to $712,500 will be due on the scheduled maturity date (which is January 1, 2019 if the interest only period is not extended, or October 1, 2019, if the interest only period is extended to March 1, 2017), or at such time the outstanding amount under the Loan Agreement is prepaid or on such earlier date the outstanding amount under the Loan Agreement becomes due and payable as specified in the Loan Agreement. If we elect to prepay the outstanding amount under the Loan Agreement prior to maturity, a prepayment charge of 3.0%, 2.0% or 1.0% of the then outstanding principal balance also will be due, depending upon whether we prepay in year 1, year 2 or after year 2 of the closing date.

Our obligations under the Loan Agreement are secured by a security interest in substantially all of our assets, excluding our intellectual property but including the proceeds from the sale, licensing or other disposition of our intellectual property.

The Loan Agreement includes customary representations, warranties and 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 stock or other equity securities; 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 business organization, in each case subject to exceptions. In addition, 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 Loan Agreement does not however include any financial maintenance covenants. The Loan Agreement also includes standard events of default, including payment defaults, breaches of covenants following any applicable cure period, a material impairment in the perfection or

priority of Hercules security interest or in the value of the collateral, the occurrence of any event that Hercules interprets as a material adverse effect (as defined in the Loan Agreement) and events relating to bankruptcy or insolvency. Upon the occurrence of an event of default, Hercules may declare all outstanding obligations immediately due and payable and take such other actions as are set forth in the Loan Agreement.

Issuance of Warrant to Lender

In connection with the Loan Agreement, on August 11, 2015, we entered into a Warrant Agreement with and issued a warrant to Hercules Technology III, L.P. evidencing the right to purchase shares of our common stock at an exercise price of $0.41 per share (the “Warrant”). The Warrant initially is exercisable for 853,658 shares of our common stock. If we elect to draw Tranche 2, then on the date we receive the additional advance, the Warrant automatically will become exercisable for an additional 426,829 shares. The exercise price and the number of shares underlying the Warrant are subject to adjustment in the event of a merger event, reclassification of our common stock, subdivision or combination of our common stock, or certain dividend payments. The Warrant is exercisable until August 11, 2020. 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.

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 12, 2015 By: /s/ Brian M. Culley
Brian M. Culley

Chief Executive Officer

(Principal Executive Officer)

By: /s/ Brandi L. Roberts
Brandi L. Roberts

Chief Financial Officer and Senior Vice President

(Principal Financial and Accounting Officer)

(46)

EXHIBIT INDEX

Exhibit No.	Description	Filed Herewith	Incorporated by Reference		
			Form	File/Film No.	Date Filed
10.1#	Mast Therapeutics, Inc. 2015 Omnibus Incentive Plan		Form 8-K	001-32157-15934477	06/16/15
10.2#	Form of Non-Statutory Stock Option Grant Agreement—Director (for grants to non-employee directors) under the 2015 Omnibus Incentive Plan		Form 8-K	001-32157-15934477	06/16/15
10.3#	Form of Incentive Stock Option Grant Agreement – Exempt Employees under the 2015 Omnibus Incentive Plan		Form 8-K	001-32157-15934477	06/16/15
10.4	Form of Incentive Stock Option Grant Agreement – Non-Exempt Employees under the 2015 Omnibus Incentive Plan		Form 8-K	001-32157-15934477	06/16/15
10.5#	Form of CEO Incentive Stock Option Grant Agreement under the 2015 Omnibus Incentive Plan		Form 8-K	001-32157-15934477	06/16/15
10.6#	Form of CMO Incentive Stock Option Grant Agreement under the 2015 Omnibus Incentive Plan		Form 8-K	001-32157-15934477	06/16/15
10.7#	2015 Executive Incentive Plan		Form 8-K	001-32157-15934477	06/16/15
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.