

Mast Therapeutics, Inc.  
Form 424B5  
August 21, 2015  
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Filed Pursuant to Rule 424(b)(5)  
Registration No. 333-202960

## PROSPECTUS SUPPLEMENT

(To Prospectus dated August 19, 2015)

**\$30,000,000**

### Common Stock

We have entered into a sales agreement, or the sales agreement, with Cowen and Company, LLC, or Cowen, relating to shares of our common stock, \$0.001 par value per share, offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$30,000,000.

Our common stock is listed on NYSE MKT under the symbol MSTX. The last reported sale price of our common stock on August 19, 2015 was \$0.46 per share.

Upon our delivery of a placement notice and subject to the terms and conditions of the sales agreement, Cowen may sell our common stock by methods deemed to be an at the market offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on the NYSE MKT, on any other existing trading market for our common stock or to or through a market maker. In addition, with our prior written approval, Cowen may also sell our common stock by any other method permitted by law, including in negotiated transactions. Cowen will act as sales agent using its commercially reasonable efforts consistent with its normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of the NYSE MKT.

We will pay Cowen a commission, or allow a discount, for its services in acting as agent in the sale of our common stock in an amount up to 3.0% of the gross sales price per share of all shares sold through it as agent under the sales agreement.

**Investing in our securities involves a high degree of risk. See Risk Factors, beginning on page S-4 of this prospectus supplement, as well as the documents incorporated by reference in this prospectus supplement, for a discussion of the factors you should carefully consider before deciding to purchase our securities.**

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

Cowen and Company

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**The date of this prospectus supplement is August 21, 2015**

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**ABOUT THIS PROSPECTUS SUPPLEMENT**

This document is in two parts. The first part is the prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, provides more general information. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, as well as the additional information described under **Where You Can Find Additional Information** on page S-8 of this prospectus supplement. These documents contain information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document filed after the date of this prospectus supplement and incorporated by reference in this prospectus supplement and the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectuses we may provide to you in connection with this offering. We have not, and Cowen has not, authorized any other person to provide you with any information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement outside the United States. This prospectus supplement does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

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**PROSPECTUS SUPPLEMENT SUMMARY**

*This summary highlights selected information about us, this offering and information appearing elsewhere in this prospectus supplement and in the documents we incorporate by reference. This summary is not complete and does not contain all the information you should consider before investing in our common stock pursuant to this prospectus supplement and the accompanying prospectus. Before making an investment decision, to fully understand this offering and its consequences to you, you should carefully read this entire prospectus supplement and the accompanying prospectus, including Risk Factors beginning on page S-4 of this prospectus supplement and the financial statements and related notes and the other information that we incorporated by reference herein, including our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q that we file from time to time.*

*Unless the context otherwise requires, all references in this prospectus to Mast, we, us, our, the Company or similar words refer to Mast Therapeutics, Inc., together with our consolidated subsidiaries.*

**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 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 losses from operations of \$29.3 million and \$21.5 million for the years ended December 31, 2014 and December 31, 2013, respectively. 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.

**Corporate Information**

In March 2013, we changed our name from ADVENTRX Pharmaceuticals, Inc. to Mast Therapeutics, Inc.

Our principal executive offices are located at 3611 Valley Centre Drive, Suite 500, San Diego, CA 92130 and our telephone number at that address is (858) 552-0866. Our corporate website is located at [www.masttherapeutics.com](http://www.masttherapeutics.com). We make available free of charge through our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The information contained in, or that can be accessed through, our website is not part of this prospectus supplement.

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**THE OFFERING**

Common stock offered by us	Shares having an aggregate offering price up to \$30,000,000.
Manner of offering	At the market offering that may be made from time to time through our agent, Cowen and Company, LLC. See Plan of Distribution on page S-7.
Use of proceeds	We plan to use the net proceeds from this offering for working capital and general corporate purposes, which include, but are not limited to, funding our ongoing and future clinical studies. Please see Use of Proceeds on page S-6.
Risk factors	See Risk Factors beginning on page S-4 of this prospectus supplement, as well as the other information included in or incorporated by reference in this prospectus supplement and the accompanying prospectus, for a discussion of risks you should carefully consider before investing in our securities.
NYSE MKT symbol	MSTX



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**RISK FACTORS**

*Investing in our securities involves a high degree of risk and uncertainty. In addition to the other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus, you should carefully consider the risks described in the Risk Factors section of our Quarterly Report on Form 10-Q for the period ended June 30, 2015, which is incorporated by reference herein, before making an investment decision with respect to the securities. We expect to update these Risk Factors from time to time in the periodic and current reports that we file with the SEC after the date of this prospectus supplement. These updated Risk Factors will be incorporated by reference in this prospectus supplement and the accompanying prospectus. Please refer to these subsequent reports for additional information relating to the risks associated with investing in our common stock. If any of such risks and uncertainties actually occurs, our business, financial condition, and results of operations could be severely harmed. This could cause the trading price of our common stock to decline, and you could lose all or part of your investment.*

**Risks Related to this Offering**

*Resales of our common stock in the public market during this offering by our stockholders may cause the market price of our common stock to fall.*

We may issue common stock from time to time in connection with this offering. The issuance from time to time of these new shares of our common stock, or our ability to issue new shares of common stock in this offering, could result in resales of our common stock by our current stockholders concerned about the potential dilution of their holdings. In turn, these resales could have the effect of depressing the market price for our common stock.

*There may be future sales or other dilution of our equity, which may adversely affect the market price of our common stock.*

We are generally not restricted from issuing additional common stock, including any securities that are convertible into or exchangeable for, or that represent the right to receive, common stock. The market price of our common stock could decline as a result of sales of common stock or securities that are convertible into or exchangeable for, or that represent the right to receive, common stock after this offering or the perception that such sales could occur.

*Our management will have broad discretion over the use of the net proceeds from this offering, you may not agree with how we use the proceeds and the proceeds may not be invested successfully.*

We have not designated any portion of the net proceeds from this offering to be used for any particular purpose. Accordingly, our management will have broad discretion as to the use of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of commencement of this offering. Accordingly, you will be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that, pending their use, we may invest the net proceeds in a way that does not yield a favorable, or any, return for our company.

*You may experience immediate and substantial dilution in the book value per share of the common stock you purchase.*

Because the prices per share at which shares of our common stock are sold in this offering may be substantially higher than the book value per share of our common stock, you may suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. The shares sold in this offering, if any, will be

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sold from time to time at various prices. After giving effect to the sale of our common stock in the maximum aggregate offering amount of \$30,000,000 at an assumed offering price of

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\$0.46 per share, the last reported sale price of our common stock on the NYSE MKT on August 19, 2015 and after deducting estimated offering commissions and expenses payable by us, our net tangible book value as of June 30, 2015 would have been \$60.0 million, or \$0.26 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.07 per share to our existing stockholders and an immediate and substantial dilution in as-adjusted net tangible book value of \$0.20 per share to new investors who purchase our common stock in the offering. See [Dilution](#) for a more detailed discussion of the dilution you may incur in connection with this offering.

**SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This prospectus supplement and our SEC filings that are incorporated by reference into this prospectus supplement contain or incorporate by reference forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. All statements, other than statements of historical fact, included or incorporated by reference in this prospectus supplement regarding our development of our products, financial position, strategy, regulatory status, clinical and nonclinical studies, collaborations, commercial prospects, internal growth, competition, intellectual property, regulatory reforms, products, objectives of management, and compliance with NYSE MKT listing standards are forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

the initiation, scope, rate of progress, results and timing of our clinical and nonclinical studies of our product candidates, including vepoloxamer;

the successful completion of our development programs and our ability to manage costs and timelines associated with clinical and nonclinical development of our product candidates, including vepoloxamer;

our ability to obtain and maintain regulatory approvals of our product candidates, including vepoloxamer;

our ability to commercialize and achieve market acceptance of our product candidates, including vepoloxamer;

our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others;

our estimates regarding the sufficiency of our cash resources and our need for additional funding; and

our intended use of the net proceeds from offerings of our securities under this prospectus supplement.

The words believe, anticipate, estimate, plan, expect, intend, may, could, should, potential, likely, will, and would and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements reflect our current views with respect to future events, are based on assumptions and are subject to risks and uncertainties. We cannot guarantee that we actually will achieve the plans, intentions or expectations expressed in our forward-looking statements and

you should not place undue reliance on these statements. There are a number of important factors that could cause our actual results to differ materially from those indicated or implied by forward-looking statements. These important factors include those discussed under the heading **Risk Factors** contained or incorporated in this prospectus supplement and the accompanying prospectus and any free writing prospectus we may authorize for use in connection with a specific offering. These factors and the other cautionary statements made in this prospectus supplement and the accompanying prospectus should be read as being applicable to all related forward-looking statements whenever they appear in this prospectus supplement and the accompanying prospectus. Except as required by law, we do not assume any obligation to update any forward-looking statement. We disclaim any intention or obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.

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We will have broad discretion in the use of the net proceeds from any sale of securities offered under this prospectus supplement. We intend to use the net proceeds for working capital and general corporate purposes, which include, but are not limited to, the funding of clinical development of and pursuing regulatory approval for our product candidates, general and administrative expenses, and the acquisition of companies, businesses or assets.

We have not determined the amount of net proceeds to be used specifically for such purposes. Pending the use of any net proceeds, we expect to invest the net proceeds in interest-bearing, marketable securities.

**DILUTION**

If you invest in our common stock, your interest will be diluted immediately to the extent of the difference between the public offering price per share and the adjusted net tangible book value per share of our common stock after this offering.

The net tangible book value of our common stock as of June 30, 2015, was approximately \$31.0 million, or approximately \$0.19 per share. Net tangible book value per share represents the amount of our total tangible assets, excluding goodwill and intangible assets, less total liabilities, divided by the total number of shares of our common stock outstanding. Dilution per share to new investors represents the difference between the amount per share paid by purchasers for each share of common stock in this offering and the net tangible book value per share of our common stock immediately following the completion of this offering.

After giving effect to the sale of shares of our common stock in the aggregate amount of \$30,000,000 at an assumed offering price of \$0.46 per share, the last reported sale price of our common stock on August 19, 2015 on the NYSE MKT, and after deducting estimated commissions and estimated offering expenses, our as-adjusted net tangible book value as of June 30, 2015 would have been approximately \$60.0 million or approximately \$0.26 per share. This represents an immediate increase in net tangible book value of approximately \$0.07 per share to our existing stockholders and an immediate dilution in as-adjusted net tangible book value of approximately \$0.20 per share to purchasers of our common stock in this offering, as illustrated by the following table:

Assumed offering price per share		\$ 0.46
Net tangible book value per share as of June 30, 2015	\$ 0.19	
Increase per share attributable to this offering	\$ 0.07	
As-adjusted net tangible book value per share as of June 30, 2015, after giving effect to this offering		\$ 0.26
Dilution per share to new investors participating in this offering		\$ 0.20

The table above assumes, for illustrative purposes only, an aggregate of 65,217,391 shares of our common stock are sold at a price of \$0.46 per share, for aggregate gross proceeds of \$30,000,000. The shares, if any, sold in this offering will be sold from time to time at various prices. An increase of \$0.10 per share in the price at which the shares are sold from the assumed offering price of \$0.46 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$30,000,000 is sold at that price, would increase the our adjusted net tangible book value per share after the offering to \$0.28 per share and increase the dilution in net tangible book value per share to new investors in this offering to \$0.28 per share, after deducting commissions and estimated aggregate offering expenses

payable by us. A decrease of \$0.10 per share in the price at which the shares are sold from the assumed offering price of \$0.46 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$30,000,000 is sold at that price, would decrease

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the adjusted net tangible book value per share after the offering to \$0.24 per share and decrease the dilution in net tangible book value per share to new investors in this offering to \$0.12 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

The table above is based on 163,614,297 shares of our common stock outstanding as of June 30, 2015 and excludes:

13,081,428 shares of our common stock issuable upon exercise of pre-funded warrants outstanding as of June 30, 2015, with an exercise price of \$0.01 per share;

62,779,804 shares of our common stock issuable upon exercise of warrants outstanding as of June 30, 2015, with a weighted-average exercise price of \$0.83 per share;

22,455,269 shares of our common stock issuable upon exercise of options outstanding as of June 30, 2015, with a weighted-average exercise price of \$0.82 per share;

22,049,559 shares of our common stock available for future grants under our 2015 Omnibus Incentive Plan as of June 30, 2015; and

12,478,050 shares of common stock that may be issued to the former stockholders of SynthRx, Inc., subject to the achievement of performance milestones, pursuant to the terms of the merger agreement with SynthRx. To the extent that any outstanding options or warrants are exercised, new options are issued under our equity incentive plan, shares of common stock are sold under our employee stock purchase plan or we otherwise issue additional shares of common stock in the future at prices per share below the price per share for any shares sold in this offering, there will be further dilution to new investors.

**PLAN OF DISTRIBUTION**

We have entered into a sales agreement with Cowen and Company, LLC, or Cowen, under which we may issue and sell from time to time shares of our common stock having an aggregate offering price of up to \$30,000,000 through Cowen as our sales agent. The form of sales agreement will be filed as an exhibit to a current report on Form 8-K and incorporated by reference in this prospectus supplement. Sales of the common stock, if any, will be made at market prices by any method permitted by law deemed to be an at the market offering as defined in Rule 415 under the Securities Act, including sales made through the NYSE MKT and any other existing trading market for the common stock, or to or through a market maker. In addition, with our express authorization, Cowen may also sell our common stock in negotiated transactions.

Cowen will offer the common stock subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and Cowen. We will designate the maximum amount of common stock to be sold through Cowen on a daily basis or otherwise determine such maximum amount together with Cowen. Subject to the terms and conditions of the sales agreement, Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. We or Cowen may suspend the

offering of the common stock being made through Cowen under the sales agreement upon proper notice to the other party. We and Cowen each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party's sole discretion at any time.

The aggregate compensation payable to Cowen as sales agent will be up to 3.0% of the gross proceeds from the sales of our common stock pursuant to the sales agreement.

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The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such common stock.

Cowen will provide written confirmation to us following the close of trading on the NYSE MKT as applicable, each day in which common stock is sold through it as sales agent under the sales agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the gross sales price per share, the net proceeds to us and the compensation payable by us to Cowen.

We will report at least quarterly the number of shares of common stock sold through Cowen under the sales agreement, the net proceeds to us and the compensation paid by us to Cowen in connection with the sales of common stock.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the third business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sales of the common stock on our behalf, Cowen may be deemed to be an underwriter within the meaning of the Securities Act, and the compensation paid to Cowen may be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to Cowen against certain liabilities, including liabilities under the Securities Act. In addition, we have agreed, under certain circumstances, to reimburse a portion of the expenses of Cowen incurred in connection with this offering up to a maximum of \$30,000. As sales agent, Cowen will not engage in any transactions that stabilize our common stock.

We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the sales agreement, will be approximately \$170,000.

## **LEGAL MATTERS**

The validity of the securities offered hereby will be passed upon for us by DLA Piper LLP (US), San Diego, California. Cowen and Company, LLC is being represented in connection with this offering by LeClairRyan, A Professional Corporation, New York, New York.

## **EXPERTS**

The consolidated financial statements incorporated in this prospectus supplement by reference to the Annual Report on Form 10-K for the year ended December 31, 2014 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of such firm as experts in auditing and accounting.

## **WHERE YOU CAN FIND ADDITIONAL INFORMATION**

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy any reports, statements and other information filed by us at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call (800) SEC-0330 for further information on the Public Reference Room. The SEC maintains an Internet website that contains reports, proxy and information statements and other information regarding issuers, including us, that file electronically with the SEC. The address for the SEC's website is <http://www.sec.gov>.

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We make available, free of charge, through our investor relations website, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, statements of changes in beneficial ownership of securities and amendments to those reports and statements as soon as reasonably practicable after they are filed with the SEC. The address for our website is <http://www.masttherapeutics.com>. The contents on our website are not part of this prospectus supplement, and the reference to our website does not constitute incorporation by reference into this prospectus supplement of the information contained at that site.

### **INCORPORATION OF CERTAIN INFORMATION BY REFERENCE**

The SEC allows us to incorporate by reference into this prospectus supplement the information we file with the SEC. This means that we can disclose important information to you by referring you to those documents. Any statement contained in a document incorporated by reference in this prospectus supplement shall be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained herein, or in any subsequently filed document, which also is incorporated by reference herein, modifies or supersedes such earlier statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

We hereby incorporate by reference into this prospectus supplement the following documents that we have filed with the SEC under the Exchange Act File No. 001-32157 (other than current reports on Form 8-K, or portions thereof, furnished under Items 2.02 or 7.01 of Form 8-K):

our Annual Report on Form 10-K for the fiscal year ended December 31, 2014, filed with the SEC on March 24, 2015 (the Annual Report ), including all material incorporated by reference therein, which includes the portions of our definitive proxy statement on Schedule 14A filed with the SEC on April 29, 2015 incorporated by reference into Part III of the Annual Report;

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2015 and June 30, 2015, filed with the SEC on May 11, 2015 and August 12, 2015, respectively;

our Current Reports on Form 8-K filed with the SEC on January 6, 2015, January 7, 2015, January 12, 2015, January 27, 2015, February 3, 2015, February 9, 2015, March 2, 2015, April 23, 2015, May 19, 2015, May 28, 2015, June 16, 2015, June 25, 2015 and August 21, 2015; and

the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on April 27, 2004 (File No. 001-32157-04755401).

All documents that we file with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act (other than current reports on Form 8-K, or portions thereof, furnished under Items 2.02 or 7.01 of Form 8-K) (i) after the initial filing date of the registration statement of which this prospectus supplement forms a part and prior to the effectiveness of such registration statement and (ii) after the date of this prospectus supplement and prior to the termination of this offering shall be deemed to be incorporated by reference in this prospectus supplement from the date of filing of the documents, unless we specifically provide otherwise. Information that we file with the SEC will automatically update and may replace information previously filed with the SEC. To the extent that any information contained in any current report on Form 8-K or any exhibit thereto, was or is furnished to, rather than filed with the SEC, such

information or exhibit is specifically not incorporated by reference.

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Upon written or oral request made to us at the address or telephone number below, we will, at no cost to the requester, provide to each person, including any beneficial owner, to whom this prospectus supplement is delivered, a copy of any or all of the information that has been incorporated by reference in this prospectus supplement (other than an exhibit to a filing, unless that exhibit is specifically incorporated by reference into that filing), but not delivered with this prospectus supplement. You may also access this information on our website at [www.masttherapeutics.com](http://www.masttherapeutics.com) by viewing the SEC Filings subsection of the Investors menu. No additional information on our website is deemed to be part of or incorporated by reference into this prospectus supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference.

Mast Therapeutics, Inc.

3611 Valley Centre Drive, Suite 500

San Diego, CA 92130

Attn: Investor Relations

(858) 552-0866

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PROSPECTUS

**\$150,000,000**

**Common Stock**

**Preferred Stock**

**Debt Securities**

**Warrants**

**Units**

We may, from time to time in one or more offerings, offer and sell up to \$150,000,000 in the aggregate of common stock, preferred stock, debt securities, warrants to purchase common stock, preferred stock or debt securities, or any combination of the foregoing, either individually or as units comprised of one or more of the other securities.

This prospectus provides a general description of the securities we may offer. We will provide the specific terms of the securities offered in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may add, update or change information contained in this prospectus. You should read carefully this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as the documents incorporated by reference before you invest in any of our securities. **This prospectus may not be used to offer or sell any securities unless accompanied by the applicable prospectus supplement.**

Our common stock is listed on the NYSE MKT under the symbol MSTX. On March 23, 2015, the last reported sale price for our common stock was \$0.52 per share.

**Investing in our securities involves a high degree of risk. See Risk Factors on page 5 of this prospectus and in the documents incorporated by reference in this prospectus, as updated in the applicable prospectus supplement, any related free writing prospectus and other future filings we make with the Securities and Exchange Commission that are incorporated by reference into this prospectus, for a discussion of the factors you should consider carefully before deciding to purchase our securities.**

We will sell these securities directly to investors, through agents designated from time to time or to or through underwriters or dealers. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution in this prospectus. If any underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable commissions or discounts will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

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The date of this prospectus is August 19, 2015

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**ABOUT THIS PROSPECTUS**

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, under the Securities Act of 1933, as amended, or the Securities Act, using a shelf registration process. Under this shelf registration process, we may from time to time sell common stock, preferred stock, debt securities or warrants to purchase common stock, preferred stock or debt securities, or any combination of the foregoing, either individually or as units comprised of one or more of the other securities, in one or more offerings up to a total dollar amount of \$150,000,000. We have provided to you in this prospectus a general description of the securities we may offer. Each time we sell securities under this shelf registration, we will, to the extent required by law, provide a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. To the extent there is a conflict between the information contained in this prospectus and the prospectus supplement or any related free writing prospectus, you should rely on the information in the prospectus supplement or the related free writing prospectus; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document filed after the date of this prospectus and incorporated by reference into this prospectus or any prospectus supplement or any related free writing perspective—the statement in the document having the later date modifies or supersedes the earlier statement.

We have not authorized any dealer, agent or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and any accompanying prospectus supplement, or any related free writing prospectus that we may authorize to be provided to you. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or an accompanying prospectus supplement, or any related free writing prospectus that we may authorize to be provided to you. This prospectus and the accompanying prospectus supplement, if any, do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and the accompanying prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference (as our business, financial condition, results of operations and prospects may have changed since that date), even though this prospectus, any applicable prospectus supplement or any related free writing prospectus is delivered or securities are sold on a later date.

As permitted by SEC rules and regulations, the registration statement of which this prospectus forms a part includes additional information not contained in this prospectus. You may read the registration statement and the other reports we file with the SEC at its web site or at its offices described below under [Where You Can Find More Information](#).

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**SUMMARY**

*This summary highlights the information contained elsewhere in or incorporated by reference into this prospectus. Because this is only a summary, it does not contain all of the information that you should consider before investing in our securities. You should carefully read this entire prospectus, including the information contained under the heading Risk Factors, and all other information included or incorporated by reference into this prospectus in their entirety before you invest in our securities.*

*Unless the context otherwise requires, all references in this prospectus to Mast, we, us, our, the Company or similar words refer to Mast Therapeutics, Inc., together with our consolidated subsidiaries.*

**Company 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 MST-188 (vepoloxamer) Injection, our lead product 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, arterial disease (in combination with thrombolytics), and heart failure. 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 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 losses from operations of \$29.3 million and \$21.5 million for the years ended December 31, 2014 and December 31, 2013, respectively. As of December 31, 2014, we had an accumulated deficit of \$235.1 million. Our cash, cash equivalents, and investment securities were \$57.3 million as of December 31, 2014.

We continue to focus our resources primarily on the development of vepoloxamer. In May 2013, we began enrolling subjects in EPIC, a pivotal Phase 3 study of vepoloxamer in patients with sickle cell disease, and enrollment of that study is one of our top priorities. We also are enrolling patients with acute limb ischemia in a Phase 2 study of vepoloxamer in combination with recombinant tissue plasminogen activator to evaluate whether vepoloxamer improves effectiveness of thrombolytic therapy. In addition, we are planning to initiate a Phase 2 study of vepoloxamer in patients with heart failure in the third quarter of 2015. Our vepoloxamer pipeline also includes preclinical development programs in thrombotic stroke and 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.



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### **Corporate Information**

In March 2013, we changed our name from ADVENTRX Pharmaceuticals, Inc. to Mast Therapeutics, Inc.

Our principal executive offices are located at 3611 Valley Centre Drive, Suite 500, San Diego, CA 92130 and our telephone number at that address is (858) 552-0866. Our corporate website is located at [www.masttherapeutics.com](http://www.masttherapeutics.com). We make available free of charge through our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The information contained in, or that can be accessed through, our website is not part of this prospectus or any prospectus supplement.

### **The Securities We May Offer**

We may offer shares of our common stock and preferred stock, various series of debt securities and warrants to purchase any of such securities, either individually or in units, with a total value of up to \$150,000,000 from time to time under this prospectus, together with any applicable prospectus supplement and related free writing prospectus, at prices and on terms to be determined by market conditions at the time of offering. If we issue any debt securities at a discount from their original stated principal amount, then, for purposes of calculating the total dollar amount of all securities issued under this prospectus, we will treat the initial offering price of the debt securities as the total original principal amount of the debt securities. Each time we offer securities under this prospectus, we will provide offerees with a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities being offered, including, to the extent applicable:

designation or classification;

aggregate principal amount or aggregate offering price;

maturity, if applicable;

original issue discount, if any;

rates and times of payment of interest or dividends, if any;

redemption, conversion, exchange or sinking fund terms, if any;

conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;

ranking;

restrictive covenants, if any;

voting or other rights, if any; and

important United States federal income tax considerations.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

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We may sell the securities to or through underwriters, dealers or agents or directly to purchasers. We, as well as any agents acting on our behalf, reserve the sole right to accept and to reject in whole or in part any proposed purchase of securities. Each prospectus supplement will set forth the names of any underwriters, dealers or agents involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them, details regarding any over-allotment option granted to them, and net proceeds to us. The following is a summary of the securities we may offer with this prospectus.

### ***Common Stock***

As of the date of this prospectus, our amended and restated certificate of incorporation, as amended, or our certificate of incorporation, authorizes us to issue 500,000,000 shares of common stock, par value \$0.001 per share, of which 159,458,376 shares were issued and outstanding as of March 20, 2015. We may offer shares of our common stock either alone or underlying other registered securities convertible into or exercisable for our common stock. Holders of our common stock are entitled to such dividends as our board of directors may declare from time to time out of legally available funds, subject to the preferential rights of the holders of any shares of our preferred stock that are outstanding or that we may issue in the future. Currently, we do not pay any dividends on our common stock. Each holder of our common stock is entitled to one vote per share. In this prospectus, we provide a general description of, among other things, the rights and restrictions that apply to holders of our common stock.

### ***Preferred Stock***

As of the date of this prospectus, our certificate of incorporation authorizes us to issue 1,000,000 shares of preferred stock, par value \$0.001 per share, none of which are outstanding. We may issue shares of our preferred stock from time to time, in one or more series.

Any authorized and undesignated shares of preferred stock may be issued with such rights and powers as the board of directors may designate. Under our certificate of incorporation, our board of directors has the authority to issue shares of our preferred stock in one or more series and to fix or alter the rights, preferences, privileges and restrictions granted to or imposed upon any series of preferred stock. The particular terms of each class or series of preferred stock, including redemption privileges, liquidation preferences, voting rights, dividend rights and/or conversion rights, will be more fully described in the applicable prospectus supplement relating to the preferred stock offered thereby.

The rights, preferences, privileges and restrictions granted to or imposed upon any series of preferred stock that we offer and sell under this prospectus and applicable prospectus supplements will be set forth in a certificate of designation relating to the series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of any certificate of designation that describes the terms of any series of preferred stock we offer under this prospectus before the issuance of shares of that series of preferred stock. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

### ***Debt Securities***

We may offer general debt obligations, which may be secured or unsecured, senior or subordinated and convertible into shares of our common stock. In this prospectus, we refer to the senior debt securities and the subordinated debt securities together as the debt securities. We may issue debt securities under a note purchase agreement or under an indenture to be entered between us and a trustee; forms of the senior and subordinated



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indentures are included as an exhibit to the registration statement of which this prospectus is a part. The indentures do not limit the amount of securities that may be issued under it and provides that debt securities may be issued in one or more series. The senior debt securities will have the same rank as all of our other indebtedness that is not subordinated. The subordinated debt securities will be subordinated to our senior debt on terms set forth in the applicable prospectus supplement. In addition, the subordinated debt securities will be effectively subordinated to creditors and preferred stockholders of our subsidiaries. Our board of directors will determine the terms of each series of debt securities being offered. This prospectus contains only general terms and provisions of the debt securities. The applicable prospectus supplement will describe the particular terms of the debt securities offered thereby. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of debt securities being offered, as well as the complete note agreements and/or indentures that contain the terms of the debt securities. Forms of indentures have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of debt securities we offer under this prospectus will be filed as exhibits to the registration statement of which this prospectus is a part, or will be incorporated by reference from another report that we file with the SEC.

## ***Warrants***

We may offer warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue the warrants by themselves or together with common stock, preferred stock or debt securities, and the warrants may be attached to or separate from any offered securities. Our board of directors will determine the terms of the warrants. This prospectus contains only general terms and provisions of the warrants. The applicable prospectus supplement will describe the particular terms of the warrants being offered thereby. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of warrants being offered, as well as the complete form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the warrants. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

## ***Units***

We may offer units consisting of our common stock or preferred stock, debt securities and/or warrants to purchase any of these securities in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units. This prospectus contains only a summary of certain general features of the units. The applicable prospectus supplement will describe the particular features of the units being offered thereby. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.





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**RISK FACTORS**

Investing in our securities involves a high degree of risk. You should carefully consider the risk factors set forth under Risk Factors in Item 1A of our annual report on Form 10-K for the year ended December 31, 2014, which is incorporated by reference in this prospectus, together with all other information contained or incorporated by reference in this prospectus, as may be updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in any applicable prospectus supplement and in any related free writing prospectus in connection with a specific offering, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus is a part. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks and uncertainties that we do not presently know about or that we currently believe are not material may also adversely affect our business.

**SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This prospectus and our SEC filings that are incorporated by reference into this prospectus contain or incorporate by reference forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. All statements, other than statements of historical fact, included or incorporated by reference in this prospectus regarding our development of our products, financial position, strategy, regulatory status, clinical and nonclinical studies, collaborations, commercial prospects, internal growth, competition, intellectual property, regulatory reforms, products, objectives of management, and compliance with NYSE MKT listing standards are forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

the initiation, scope, rate of progress, results and timing of our clinical and nonclinical studies of

our product candidates, including vepoloxamer;

the successful completion of our development programs and our ability to manage costs associated with clinical and nonclinical development of our product candidates, including vepoloxamer;

our ability to obtain and maintain regulatory approvals of our product candidates, including vepoloxamer;

our ability to commercialize and achieve market acceptance of our product candidates, including vepoloxamer;

our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others;

our estimates regarding the sufficiency of our cash resources and our need for additional funding; and

our intended use of the net proceeds from offerings of our securities under this prospectus.

The words believe, anticipate, estimate, plan, expect, intend, may, could, should, potential, like, will, and would and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements reflect our current views with respect to future events, are based on assumptions and are subject to risks and uncertainties. We cannot guarantee that we actually will achieve the plans, intentions or expectations expressed in our forward-looking statements and you should not place undue reliance on these statements. There are a number of important factors that could cause our actual results to differ materially from those indicated or implied by forward-looking statements. These important factors include those discussed under the heading Risk Factors contained or incorporated in this prospectus and in the applicable prospectus supplement and any free writing prospectus we may authorize for use in connection with a specific offering.

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These factors and the other cautionary statements made in this prospectus should be read as being applicable to all related forward-looking statements whenever they appear in this prospectus. Except as required by law, we do not assume any obligation to update any forward-looking statement. We disclaim any intention or obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.

**USE OF PROCEEDS**

Except as described in any prospectus supplement and any free writing prospectus in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered under this prospectus to fund continued development of our product candidates, including clinical studies, nonclinical testing and research-related manufacturing activities, to pursue regulatory approval for our product candidates and, potentially, to commercialize product candidates that receive regulatory approval, and for general corporate purposes, including working capital. We may also use a portion of the net proceeds to acquire or invest in technologies, product candidates, products and/or businesses that we believe will enhance the value of our company, although we have no current commitments or agreements with respect to any such transactions as of the date of this prospectus. We have not determined the amount of net proceeds to be used specifically for the foregoing purposes. As a result, our management will have broad discretion in the allocation of the net proceeds and investors will be relying on the judgment of our management regarding the application of the proceeds of any sale of the securities. If a material part of the net proceeds is to be used to repay indebtedness, we will set forth the interest rate and maturity of such indebtedness in a prospectus supplement. Pending use of the net proceeds, we in