

Mast Therapeutics, Inc.
Form 424B5
February 10, 2014
Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-179989

PROSPECTUS SUPPLEMENT

(To Prospectus dated May 1, 2012)

\$30,000,000

Common Stock

We have entered into a 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 February 6, 2014 was \$0.81 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

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

The date of this prospectus supplement is February 10, 2014

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

<u>ABOUT THIS PROSPECTUS SUPPLEMENT</u>	S-1
<u>PROSPECTUS SUPPLEMENT SUMMARY</u>	S-2
<u>THE OFFERING</u>	S-3
<u>RISK FACTORS</u>	S-4
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	S-5
<u>USE OF PROCEEDS</u>	S-6
<u>DILUTION</u>	S-6
<u>PLAN OF DISTRIBUTION</u>	S-8
<u>LEGAL MATTERS</u>	S-9
<u>EXPERTS</u>	S-9
<u>WHERE YOU CAN FIND ADDITIONAL INFORMATION</u>	S-9
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	S-9
<u>ABOUT THIS PROSPECTUS</u>	ii
<u>SUMMARY</u>	1
<u>RISK FACTORS</u>	4
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	4
<u>RATIO OF EARNINGS TO FIXED CHARGES</u>	6
<u>USE OF PROCEEDS</u>	6
<u>SECURITIES WE MAY OFFER</u>	7
<u>DESCRIPTION OF COMMON STOCK AND PREFERRED STOCK</u>	7
<u>DESCRIPTION OF DEBT SECURITIES</u>	10
<u>DESCRIPTION OF WARRANTS</u>	16
<u>DESCRIPTION OF UNITS</u>	17
<u>LEGAL OWNERSHIP OF SECURITIES</u>	18
<u>PLAN OF DISTRIBUTION</u>	21
<u>LEGAL MATTERS</u>	23
<u>EXPERTS</u>	23
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	23
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	23

Table of Contents

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-9 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.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information about us, this offering and information appearing elsewhere in this prospectus supplement, in the accompanying prospectus 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 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, our lead product candidate, for diseases and conditions characterized by microcirculatory insufficiency (endothelial dysfunction and/or impaired blood flow).

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 \$15.8 million for the nine months ended September 30, 2013. Our cash, cash equivalents and investment securities as of December 31, 2013 were over \$44 million.

We continue to focus our resources on MST-188. We believe that its pharmacologic effects support its development in a wide range of diseases and conditions and we intend to develop MST-188 in multiple clinical indications, both independently and through collaborations. In 2013, we initiated the EPIC study, a pivotal phase 3 study of MST-188 in sickle cell disease, and enrolling subjects in that study is one of our top priorities. In addition to sickle cell disease, our MST-188 pipeline includes development programs in adjunctive thrombolytic therapy (e.g., acute limb ischemia, stroke), heart failure, and resuscitation (i.e., restoration of circulating blood volume and pressure) following major trauma. We plan to initiate a phase 2, clinical proof-of-concept study in acute limb ischemia that will evaluate whether MST-188 improves the effectiveness of existing thrombolytic agents in early 2014.

Corporate Information

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

Our principal executive offices are located at 12390 El Camino Real, Suite 150, San Diego, CA 92130 and our telephone number is (858) 552-0866.

Table of Contents

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-8.
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

Table of Contents

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 Form 10-Q for the quarter ended June 30, 2013, 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

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 \$0.81 per share, the last reported sale price of our common stock on the NYSE MKT on February 6, 2014, and after deducting estimated offering commissions and expenses payable by us, our net tangible book value as of September 30, 2013 would have been \$72.5 million, or \$0.52 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.10 per share to our existing stockholders and an immediate and substantial dilution in as-adjusted net tangible book value of \$0.29 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.

S-4

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the SEC filings that are incorporated by reference into this prospectus supplement and the accompanying prospectus contain or incorporate by reference forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended. All statements, other than statements of historical fact, included or incorporated by reference in this prospectus supplement or the accompanying 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. The words believe, anticipate, estimate, plan, expect, intend, may, could, should, potential, likely, projects, continue, will, and would and similar expressions are used to identify forward-looking statements, although not all forward-looking statements contain these identifying words. 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 our forward-looking 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 set forth above under Risk Factors. These factors and the other cautionary statements made in this prospectus supplement 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.

Table of Contents**USE OF PROCEEDS**

We will have broad discretion in the use of the net proceeds from any sale of securities offered under this prospectus supplement and the accompanying prospectus. We intend to use the net proceeds for working capital and general corporate purposes, which include, but are not limited to, the funding of research and product development activities including our ongoing and future nonclinical and clinical trials, 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 September 30, 2013, was approximately \$43.5 million, or approximately \$0.42 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 \$0.81 per share, the last reported sale price of our common stock on February 6, 2014 on the NYSE MKT, and after deducting estimated commissions and estimated offering expenses, our as-adjusted net tangible book value as of September 30, 2013 would have been approximately \$72.5 million or approximately \$0.52 per share. This represents an immediate increase in net tangible book value of approximately \$0.10 per share to our existing stockholders and an immediate dilution in as-adjusted net tangible book value of approximately \$0.29 per share to purchasers of our common stock in this offering, as illustrated by the following table:

Assumed offering price per share	\$ 0.81
Net tangible book value per share as of September 30, 2013	\$ 0.42
Increase per share attributable to this offering	\$ 0.10
As-adjusted net tangible book value per share as of September 30, 2013, after giving effect to this offering	\$ 0.52
Dilution per share to new investors participating in this offering	\$ 0.29

The table above assumes, for illustrative purposes only, an aggregate of 37,037,037 shares of our common stock are sold at a price of \$0.81 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 \$0.20 per share in the price at which the shares are sold from the assumed offering price of \$0.81 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 adjusted net tangible book value per share after the offering to \$0.55 per share and increase the dilution in net tangible book value per share to new investors in this offering to \$0.46 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$0.20 per share in the price at which the shares are sold from the assumed offering price of \$0.81 per

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

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 the adjusted net tangible book value per share after the offering to \$0.48 per share and decrease the dilution in net tangible book value per share to new investors in this offering to \$0.13 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

S-6

Table of Contents

The above table is based on 102,710,286 shares of our common stock outstanding as of September 30, 2013 and excludes, as of September 30, 2013:

44,585,932 shares of our common stock issuable upon exercise of outstanding warrants, with a weighted-average exercise price of \$1.07 per share;

12,478,050 shares of common stock that may be issued to the former stockholders of SynthRx, subject to the achievement of performance milestones, pursuant to the terms of the merger agreement with SynthRx;

7,148,103 shares of our common stock issuable upon exercise of outstanding options, with a weighted-average exercise price of \$1.41 per share; and

3,407,947 shares and 276,945 shares of our common stock available for future grants under our 2013 Omnibus Incentive Plan and 2005 Employee Stock Purchase Plan, respectively.

To the extent that any options or warrants are exercised, new options are issued under our equity incentive plan, additional 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.

Table of Contents

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 privately 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.

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 \$230,000.

S-8

Table of Contents

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 as of December 31, 2012 and December 31, 2011 and for each of the two years in the period ended December 31, 2012, and cumulatively, for the period January 1, 2011 to December 31, 2012 incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2012 have been so included in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

The consolidated statements of operations and comprehensive income/(loss), stockholders' equity (deficit) and cash flows for the period from January 1, 2002 through December 31, 2010 are incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2012 in reliance upon the report of CohnReznick LLP, an independent registered public accounting firm, given on the authority of such firm as an expert in accounting and auditing.

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>.

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, and the reference to our website does not constitute incorporation by reference into this prospectus of the information contained at that site.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to another document that we have filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus supplement. We incorporate by reference the following information or documents that we have filed with the SEC (excluding those portions of any Form 8-K that are not deemed filed pursuant to the General Instructions of Form 8-K):

Our Quarterly Report on Form 10-Q for the quarter ended September 30, 2013, filed with the SEC on November 4, 2013;

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2013, filed with the SEC on August 5, 2013;

Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2013, filed with the SEC on May 15, 2013;

Our Annual Report on Form 10-K for the year ended December 31, 2012, filed with the SEC on March 19, 2013;

Our Current Reports on Form 8-K filed with the SEC on January 3, 2013, February 8, 2013, February 26, 2013, March 1, 2013, March 12, 2013, June 17, 2013, June 21, 2013, as amended by our Form 8-K/A filed with the SEC on October 30, 2013, August 9, 2013, January 8, 2014 and February 10, 2014;

S-9

Table of Contents

The portions of our definitive proxy statement on Schedule 14A, filed with the SEC on April 29, 2013, that are incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2012; 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 reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and deemed to be part of this prospectus supplement from the date of the filing of such reports and documents.

Any statement contained in any document incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or any additional prospectus supplements modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

We will provide without charge to each person, including any beneficial owner, to whom this prospectus supplement is delivered, upon written or oral request, a copy of any or all documents that are incorporated by reference into this prospectus supplement, but not delivered with the prospectus supplement, other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the documents that this prospectus supplement incorporates. You should direct written requests to: Mast Therapeutics, Inc., 12390 El Camino Real, Suite 150, San Diego, California 92130, Attn: Investor Relations, or you may call us at (858) 552-0866.

Table of Contents

PROSPECTUS

\$150,000,000

Common Stock

Preferred Stock

Debt Securities

Warrants

Units

ADVENTRX PHARMACEUTICALS, INC.

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 Amex equities market under the symbol ANX. On March 7, 2012 the last reported sale price for our common stock was \$0.63 per share. The aggregate market value of our outstanding shares of common stock held by non-affiliates is approximately \$29.7 million, based on 47,168,046 outstanding shares held by non-affiliates as of March 5, 2012 and the last reported sale price per share of our common stock on the NYSE Amex equities market on March 7, 2012. We have not offered any securities pursuant to General Instruction I.B.6. of Form S-3 during the prior 12 calendar month period that ends on, and includes, the date of this prospectus.

Investing in our securities involves a high degree of risk. See Risk Factors on page 4 of this prospectus and 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.

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

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

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.

The date of this prospectus is May 1, 2012.

Table of Contents

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	ii
<u>SUMMARY</u>	1
<u>RISK FACTORS</u>	4
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	4
<u>RATIO OF EARNINGS TO FIXED CHARGES</u>	6
<u>USE OF PROCEEDS</u>	6
<u>SECURITIES WE MAY OFFER</u>	7
<u>DESCRIPTION OF COMMON STOCK AND PREFERRED STOCK</u>	7
<u>DESCRIPTION OF DEBT SECURITIES</u>	10
<u>DESCRIPTION OF WARRANTS</u>	16
<u>DESCRIPTION OF UNITS</u>	17
<u>LEGAL OWNERSHIP OF SECURITIES</u>	18
<u>PLAN OF DISTRIBUTION</u>	21
<u>LEGAL MATTERS</u>	23
<u>EXPERTS</u>	23
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	23
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	23

Table of Contents

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 incorporated by reference in this prospectus or any prospectus supplement or any related free writing prospectus—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. 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 the rules and regulations of the SEC, 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 the SEC's web site or at the SEC's offices described below under the heading **Where You Can Find Additional Information**.

Trademarks, Trade Names and Service Marks

We own or have rights to use the trademarks, service marks and trade names that we use in conjunction with the operation of our business. Some of the more important trademarks that we own or have rights to use that appear in this prospectus include: Exelbine and SYNTHRAX®, which are registered or trademarked in the United States. Each trademark, trade name or service mark of any other company appearing in this prospectus is, to our knowledge, owned by such other company.

Company References

In this prospectus, unless otherwise specified or the context otherwise requires, references to ADVENTRX Pharmaceuticals, Inc., ADVENTRX, we, us, our and our company refer to ADVENTRX Pharmaceuticals, Inc. and its consolidated subsidiaries.

Table of Contents

SUMMARY

This summary highlights selected information from this prospectus and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, including the section entitled Risk Factors on page 4, the information incorporated herein by reference, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

About ADVENTRX Pharmaceuticals, Inc.

We are a biopharmaceutical company focused on developing proprietary product candidates. Our lead product candidate is ANX-188, a rheologic, antithrombotic and cytoprotective agent that improves microvascular blood flow and has potential application in treating a wide range of diseases and conditions, such as complications arising from sickle cell disease. We also are developing ANX-514, a novel, detergent-free formulation of the chemotherapy drug docetaxel.

We are a development-stage company and have not yet marketed or sold any products or generated any significant revenue. We have devoted substantially all of our resources to research and development and to acquisition of our product candidates. We have incurred significant losses since inception and we incurred a loss from operations of \$13.4 million for the year ended December 31, 2011. We had cash, cash equivalents and short-term investments of \$50.7 million at December 31, 2011.

Our company was incorporated in Delaware in December 1995. In October 2000, we merged our wholly-owned subsidiary, Biokeys Acquisition Corp., with and into Biokeys, Inc. and changed our name to Biokeys Pharmaceuticals, Inc. In May 2003, we merged Biokeys, Inc., our wholly owned subsidiary, with and into us and changed our name to ADVENTRX Pharmaceuticals, Inc. In April 2006, we acquired SD Pharmaceuticals, Inc., a Delaware corporation, and, in April 2011, we acquired SynthRx, Inc., a Delaware corporation, each as a wholly-owned subsidiary through a merger transaction.

Our executive offices are located at 12390 El Camino Real, Suite 150, San Diego, California 92130, and our telephone number is (858) 552-0866. Our corporate website is located at www.adventrx.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;

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

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;

Table of Contents

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.

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. 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 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

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

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

Table of Contents

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. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. 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 warrant agreements that contain the terms of the warrants. Specific warrant 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 warrant agreement relating to warrants offered under this prospectus.

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.

Table of Contents

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, 2011, 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the other materials we have filed or will file with the SEC that are incorporated by reference herein contain 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, are statements that could be deemed forward-looking statements, including, but not limited to, statements regarding our business strategy, expectations and plans, our objectives for future operations and our future financial position. When used in this prospectus or in the other materials we have filed or will file with the SEC, the words *believe*, *may*, *could*, *will*, *estimate*, *continue*, *anticipate*, *intend*, *indicate*, *seek*, *should* or *would* and similar expressions are intended to identify forward-looking statements. Among the factors that could cause or contribute to material differences between our actual results and those indicated from the forward-looking statements are risks and uncertainties inherent in our business, including, but not limited to:

our ability, or that of a future partner, to successfully develop and obtain regulatory approval for, and then successfully commercialize our product candidates in the U.S. and/or elsewhere;

our ability to obtain additional funding to develop our product candidates on a timely basis or on acceptable terms, or at all;

the potential for us to delay, reduce or discontinue current and/or planned development activities, partner our product candidates at inopportune times or pursue less expensive but higher-risk development paths if we are unable to raise sufficient additional capital as needed;

delays in the commencement or completion of a clinical study or manufacturing and regulatory activities related to our product candidates;

suspension or termination of a clinical study;

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 our product candidates and certain of their component materials 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 contract research organizations, on whom we rely significantly to conduct our nonclinical testing, clinical studies and other aspects of our development programs;

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

the extent of market acceptance of any of our product candidates for which we receive regulatory approval;

the extent to which we acquire new technologies and/or product candidates and our ability to integrate them successfully into our operations;

the potential that we may enter into one or more commercial partnerships or other strategic transactions relating to our product candidates, and the terms of any such transactions;

the extent to which we increase our workforce and our ability to attract and retain qualified personnel and manage growth;

competition in the marketplace for our products, if any are approved;

our ability to protect our intellectual rights with respect to our product candidates and proprietary technology;

Table of Contents

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 our products' commercial success;

undesirable side effects that our product candidates may cause;

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

our ability to maintain compliance with NYSE Amex continued listing standards and maintain the listing of our common stock on the NYSE Amex or another national securities exchange.

Additional factors that could cause or contribute to such differences include, but are not limited to, those discussed in this prospectus, and in particular, the risks discussed under the heading "Risk Factors" in this prospectus and those discussed in other documents we file with the SEC and incorporate herein. Except as required by law, we do not intend to update these forward-looking statements 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, uncertainties and assumptions, the forward-looking events and circumstances discussed in this prospectus and in the documents incorporated in this prospectus may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Accordingly, readers are cautioned not to place undue reliance on such forward-looking statements.

Table of Contents**RATIO OF EARNINGS TO FIXED CHARGES**

The following table sets forth, for the periods presented, our ratio of earnings to fixed charges and our ratio of earnings to combined fixed charges and preferred stock dividends. For purposes of computing the ratio of earnings to fixed charges and the ratio of earnings to combined fixed charges and preferred stock dividends, earnings consist of net loss plus fixed charges. Fixed charges consist of interest expense and an estimate of the interest component of rent expense. In each of the periods presented, earnings were insufficient to cover fixed charges and combined fixed charges and deemed dividends on preferred stock and the extent of such deficiencies in each period is shown below.

	Year Ended December 31,				
	2011	2010	2009	2008	2007
Ratio of earnings to fixed charges	\$	\$	\$	\$	\$
Deficiency of earnings available to cover fixed charges	\$ (13,259,931)	\$ (8,450,922)	\$ (11,325,058)	\$ (26,647,493)	\$ (22,142,040)
Ratio of earnings to combined fixed charges and preferred stock dividends	\$	\$	\$	\$	\$
Deficiency of earnings available to cover combined fixed charges and preferred stock dividends	\$ (13,259,931)	\$ (14,090,718)	\$ (16,191,945)	\$ (26,647,493)	\$ (22,142,040)

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. Pending use of the net proceeds, we intend to invest the proceeds in short-term, investment-grade, interest-bearing instruments.

Each time we offer securities under this prospectus, we will describe the intended use of the net proceeds from that offering in the applicable prospectus supplement. The actual amount of net proceeds we spend on a particular use will depend on many factors, including, our future capital expenditures, the amount of cash required by our operations, and our future revenue growth, if any. Therefore, we will retain broad discretion in the use of the net proceeds.

Table of Contents

SECURITIES WE MAY OFFER

We may offer shares of common stock, shares of 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. We may offer up to \$150,000,000 of securities under this prospectus. If securities are offered as units, we will describe the terms of the units in a prospectus supplement.

DESCRIPTION OF COMMON STOCK AND PREFERRED STOCK

The following description of our common stock and preferred stock, together with any additional information we include in any applicable prospectus supplement or any related free writing prospectus, summarizes the material terms and provisions of our common stock and the preferred stock that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future common stock or preferred stock that we may offer, we will describe the particular terms of any class or series of these securities in more detail in the applicable prospectus supplement. For the complete terms of our common stock and preferred stock, please refer to our certificate of incorporation and our amended and restated bylaws, or bylaws, that are incorporated by reference into the registration statement of which this prospectus is a part or may be incorporated by reference in this prospectus or any applicable prospectus supplement. The terms of these securities may also be affected by Delaware General Corporation Law. The summary below and that contained in any applicable prospectus supplement or any related free writing prospectus are qualified in their entirety by reference to our certificate of incorporation and bylaws, as in effect at the time of any offering of securities under this prospectus.

Common Stock

As of the date of this prospectus, our certificate of incorporation authorizes us to issue 500,000,000 shares of common stock, par value \$0.001 per share, of which 47,715,709 shares were issued and outstanding as of March 5, 2012. Additional shares of authorized common stock may be issued, as authorized by our board of directors from time to time, without stockholder approval, except as may be required by applicable securities exchange requirements. The holders of common stock possess exclusive voting rights in us, except to the extent our board of directors specifies voting power with respect to any other class of securities issued in the future. Each holder of our common stock is entitled to one vote for each share held of record on each matter submitted to a vote of stockholders, including the election of directors. Stockholders do not have any right to cumulate votes in the election of directors.

Subject to preferences that may be granted to the holders of preferred stock, each holder of our common stock is entitled to share ratably in distributions to stockholders and to receive ratably such dividends as may be declared by our board of directors out of funds legally available therefor. In the event of our liquidation, dissolution or winding up, the holders of our common stock will be entitled to receive, after payment of all of our debts and liabilities and of all sums to which holders of any preferred stock may be entitled, the distribution of any of our remaining assets. Holders of our common stock have no conversion, exchange, sinking fund, redemption or appraisal rights (other than such as may be determined by our board of directors in its sole discretion) and have no preemptive rights to subscribe for any of our securities.

All of the outstanding shares of our common stock are fully paid and non-assessable. The shares of common stock offered by this prospectus or upon the conversion of any preferred stock or debt securities or exercise of any warrants offered pursuant to this prospectus, when issued and paid for, will also be, fully paid and non-assessable.

Securities Exchange Listing

Our common stock is listed on the NYSE Amex under the symbol ANX.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company.

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. Pursuant to our certificate of incorporation, our board of directors has the authority to provide for the issuance, in one or more series, of our authorized preferred stock and to fix or alter the rights, preferences, privileges and restrictions granted to or imposed upon any series of our preferred stock. The rights, privileges, preferences and restrictions of any such series of our preferred stock may be subordinated to, pari passu with (including, without limitation, inclusion in provisions with respect to liquidation and acquisition

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

preferences, redemption or approval of matters by vote or written consent), or senior to any of those of any present or future class or series of preferred stock or common stock. Our board of directors is also expressly authorized to increase or decrease the number of shares of any series prior or subsequent to the issue of that series, but not

Table of Contents

below the number of shares of such series then outstanding. The issuance of preferred stock may have the effect of decreasing the market price of our common stock and may adversely affect the voting power of holders of our common stock and reduce the likelihood that holders of our common stock will receive dividend payments and payments upon liquidation.

The particular terms of each class or series of preferred stock that we may offer under this prospectus, 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 of any series of preferred stock we may offer under this prospectus will be set forth in the certificate of designation relating to that series of preferred stock. 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 we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we may offer before the issuance of the related series of preferred stock. The applicable prospectus supplement will specify the particular terms of any series of preferred stock we may offer, including, but not limited to:

the distinctive designation and the maximum number of shares in the series;

the number of shares we are offering and purchase price per share;

the liquidation preference, if any;

the terms on which dividends, if any, will be paid;

the voting rights, if any, on the shares of the series;

the terms and conditions, if any, on which the shares of the series shall be convertible into, or exchangeable for, shares of any other class or classes of capital stock;

the terms on which the shares may be redeemed, if at all;

any listing of the preferred stock on any securities exchange or market;

a discussion of any material or special United States federal income tax considerations applicable to the preferred stock; and

any or all other preferences, rights, restrictions, including restrictions on transferability, and qualifications of shares of the series.

The description of preferred stock above and the description of the terms of a particular series of preferred stock in any applicable prospectus supplement are not complete. You should refer to any applicable certificate of designation for complete information.

The General Corporate Law of the State of Delaware, the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of that preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Anti-Takeover Effects of Provisions of our Charter Documents and Delaware Law

Provisions of Delaware General Corporation Law, or the DGCL, and our certificate of incorporation and bylaws could make it more difficult to acquire us by means of a tender offer, a proxy contest or otherwise, or to remove incumbent officers and directors. These provisions, summarized below, are expected to discourage certain types of coercive takeover practices and takeover bids that our board of directors may consider inadequate and to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased protection of our ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging takeover or acquisition proposals because, among other things, negotiation of these proposals could result in an improvement of their terms. This summary does not purport to be complete and is qualified in its entirety by reference to the corporate law of Delaware and our certificate of incorporation and bylaws.

Table of Contents

Certificate of Incorporation and Bylaws

Preferred Stock. Under our certificate of incorporation, our board of directors has the power to authorize the issuance of up to 1,000,000 shares of preferred stock, all of which are currently undesignated, and to determine the price, rights, preferences, privileges and restrictions, including voting rights, of those shares without further vote or action by our stockholders. The issuance of preferred stock may:

delay, defer or prevent a change in control;

discourage bids for our common stock at a premium over the market price of our common stock;

adversely affect the voting and other rights of the holders of our common stock; and

discourage acquisition proposals or tender offers for our shares and, as a consequence, inhibit fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

Advance Notice Requirement. Stockholder nominations of individuals for election to our board of directors and stockholder proposals of other matters to be brought before an annual meeting of our stockholders must comply with the advance notice procedures set forth in our bylaws. Generally, to be timely, such notice must be received at our principal executive offices no later than the date specified in our proxy statement released to stockholders in connection with the preceding year's annual meeting of stockholders, which date shall be not earlier than the 120th day, nor later than the close of business on the 90th day, prior to the first anniversary of the date of the preceding year's annual meeting of stockholders.

Special Meeting Requirements. Our bylaws provide that special meetings of our stockholders may be called only at the request of our board of directors, president (unless there is a chief executive officer who is not the president, in which case a special meeting may be called at any time by the chief executive officer and not the president) or chair of the board of directors. Only such business shall be considered at a special meeting as shall have been stated in the notice for such meeting.

No Cumulative Voting. Our certificate of incorporation does not include a provision for cumulative voting for directors.

Indemnification. Our certificate of incorporation and bylaws provide that we will indemnify our officers and directors against losses as they incur in investigations and legal proceedings resulting from their services to us, which may include service in connection with takeover defense measures.

Removal of Directors. Our bylaws provide that the affirmative vote of the holders of at least 75% of our voting stock then outstanding is required to remove our directors, either with or without cause.

Authorized but Unissued Shares. Our authorized but unissued shares of common stock and preferred stock will be available for future issuance without stockholder approval. We may use additional shares for a variety of purposes, including future public offerings to raise additional capital, to fund acquisitions and as employee compensation. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Delaware Anti-Takeover Statute.

We are subject to Section 203 of the DGCL, an anti-takeover law. In general, Section 203 prohibits, with some exceptions, a publicly held Delaware corporation from engaging in a business combination with any interested stockholder for a period of three years following the date that stockholder became an interested stockholder, unless:

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

prior to that date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;

upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares of voting stock outstanding (but not the voting stock owned by the interested stockholder) those shares owned by persons who are directors and officers and by excluding employee stock plans in which employee participants do not have the right to determine whether shares held subject to the plan will be tendered in a tender or exchange offer; or

on or subsequent to that date, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66-2/3% of the outstanding voting stock that is not owned by the interested stockholder.

Section 203 defines "business combination" to include any of the following:

any merger or consolidation involving the corporation and the interested stockholder;

Table of Contents

any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;

subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any person who, together with the person's affiliates and associates, beneficially owns, or within three years prior to the determination of interested stockholder status did beneficially own, 15% or more of the outstanding voting stock of the corporation.

The above provisions may deter a hostile takeover or delay a change in control of management or us.

DESCRIPTION OF DEBT SECURITIES

General

The debt securities that we may issue may constitute debentures, notes, bonds or other evidences of indebtedness of our company, to be issued in one or more series, which may include senior debt securities, subordinated debt securities and senior subordinated debt securities. The particular terms of any series of debt securities we may offer, including the extent to which the general terms set forth below may be applicable to a particular series, will be described in a prospectus supplement relating to such series.

Debt securities that we may issue may be issued under a senior indenture between us and a trustee, or a subordinated indenture between us and a trustee (collectively, the indentures). We have filed forms of the indentures as exhibits to the registration statement of which this prospectus is a part. Supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

THE FOLLOWING DESCRIPTION IS A SUMMARY OF THE MATERIAL PROVISIONS OF THE INDENTURES. IT DOES NOT RESTATE THE INDENTURES IN THEIR ENTIRETY. THE INDENTURES ARE GOVERNED BY THE TRUST INDENTURE ACT OF 1939. THE TERMS OF THE DEBT SECURITIES INCLUDE THOSE STATED IN THE INDENTURES AND THOSE MADE PART OF THE INDENTURES BY REFERENCE TO THE TRUST INDENTURE ACT. WE URGE YOU TO READ THE INDENTURES BECAUSE THEY, AND NOT THIS DESCRIPTION, DEFINE YOUR RIGHTS AS A HOLDER OF THE DEBT SECURITIES. EXCEPT AS WE MAY OTHERWISE INDICATE, THE TERMS OF THE SENIOR INDENTURE AND THE SUBORDINATED INDENTURE ARE IDENTICAL.

The indentures contain no covenant or provision which affords debt holders protection in the event of a highly leveraged transaction.

Information You Will Find in the Prospectus Supplement

The indentures provide that we may issue debt securities from time to time in one or more series by resolution of our board of directors or by means of a supplemental indenture, and that we may denominate the debt securities and make them payable in foreign currencies. The indentures do not limit the aggregate principal amount of debt securities that can be issued thereunder. We may specify a maximum aggregate principal amount for the debt securities of any series. We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

the title;

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;

any limit on the amount that may be issued;

Table of Contents

whether or not we will issue the series of debt securities in global form, and, if so, the terms and who the depositary will be;

the maturity date;

whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;

the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

the terms of the subordination of any series of subordinated debt;

the place where payments will be payable;

restrictions on transfer, sale or other assignment, if any;

our right, if any, to defer payment of interest and the maximum length of any such deferral period;

the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;

the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option, to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;

whether the indenture will restrict our ability or the ability of our subsidiaries to:

incur additional indebtedness;

issue additional securities;

create liens;

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries, or redeem capital stock;

place restrictions on our subsidiaries' ability to pay dividends, make distributions or transfer assets;

make investments or other restricted payments;

sell or otherwise dispose of assets;

enter into sale-leaseback transactions;

engage in transactions with stockholders or affiliates;

issue or sell stock of our subsidiaries;

effect a consolidation or merger;

whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;

a discussion of certain material or special United States federal income tax considerations applicable to the debt securities;

Table of Contents

information describing any book-entry features;

provisions for a sinking fund purchase or other analogous fund, if any;

the applicability of the provisions in the indenture on discharge;

whether the debt securities are to be offered at a price such that they will be deemed to be offered at an original issue discount as defined in paragraph (a) of Section 1273 of the Internal Revenue Code of 1986, as amended;

the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;

the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock, our preferred stock or other securities (including securities of a third-party). We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock, our preferred stock or other securities (including securities of a third-party) that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indentures will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible into or exchangeable for our other securities or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default under the Indentures

Unless otherwise indicated in the applicable prospectus supplement, the following will be events of default under the indentures with respect to each series of debt securities issued under the indenture:

if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended;

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable at maturity, upon redemption or repurchase or otherwise, and the time for payment has not been extended;

if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the trustee or we and the trustee receive notice from the holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and

if specified events of bankruptcy, insolvency or reorganization occur.

We will describe in each applicable prospectus supplement any additional events of default relating to the relevant series of debt securities.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid

Table of Contents

principal, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the unpaid principal, premium, if any, and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity or security satisfactory to it against any loss, liability or expense. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

the direction so given by the holder is not in conflict with any law or the applicable indenture; and

subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

The indentures provide that if an event of default has occurred and is continuing, the trustee will be required in the exercise of its powers to use the degree of care that a prudent person would use in the conduct of its own affairs. The trustee, however, may refuse to follow any direction that conflicts with law or the indenture, or that the trustee determines is unduly prejudicial to the rights of any other holder of the relevant series of debt securities, or that would involve the trustee in personal liability. Prior to taking any action under the indentures, the trustee will be entitled to indemnification against all costs, expenses and liabilities that would be incurred by taking or not taking such action.

A holder of the debt securities of any series will have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies only if:

the holder has given written notice to the trustee of a continuing event of default with respect to that series;

the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the trustee or security satisfactory to it against any loss, liability or expense or to be incurred in compliance with instituting the proceeding as trustee; and

the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities, or other defaults that may be specified in the applicable prospectus supplement.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indentures.

The indentures provide that if a default occurs and is continuing and is actually known to a responsible officer of the trustee, the trustee must mail to each holder notice of the default within the earlier of 90 days after it occurs and 30 days after it is known by a responsible officer of the trustee or written notice of it is received by the trustee, unless such default has been cured or waived. Except in the case of a default in the payment of principal or premium of or interest on any debt security or certain other defaults specified in an indenture, the trustee shall be protected in withholding such notice if and so long as the board of directors, the executive committee or a trust committee of directors, or responsible officers of the trustee, in good faith determine that withholding notice is in the best interests of holders of the relevant series of debt

securities.

Modification of Indenture; Waiver

Subject to the terms of the indenture for any series of debt securities that we may issue, we and the trustee may change an indenture without the consent of any holders with respect to the following specific matters:

to fix any ambiguity, defect or inconsistency in the indenture;

Table of Contents

to comply with the provisions described above under Description of Debt Securities Consolidation, Merger or Sale ;

to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act;

to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;

to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under Description of Debt Securities General, to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

to evidence and provide for the acceptance of appointment hereunder by a successor trustee;

to provide for uncertificated debt securities and to make all appropriate changes for such purpose;

to add to our covenants such new covenants, restrictions, conditions or provisions for the benefit of the holders, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred to us in the indenture; or

to change anything that does not adversely affect the interests of any holder of debt securities of any series in any material respect.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, subject to the terms of the indenture for any series of debt securities that we may issue or otherwise provided in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may only make the following changes with the consent of each holder of any outstanding debt securities affected:

extending the stated maturity of the series of debt securities;

reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption or repurchase of any debt securities; or

reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that, subject to the terms of the indenture and any limitation otherwise provided in the prospectus supplement applicable to a particular series of debt securities, we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

recover excess money held by the trustee;

compensate and indemnify the trustee; and

appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium and interest on, the debt securities of the series on the dates payments are due.

Table of Contents

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement with respect to that series. See **Legal Ownership of Securities** below for a further description of the terms relating to any book-entry securities.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture and is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur. However, upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Table of Contents

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Ranking Debt Securities

The subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

The senior debt securities will be unsecured and will rank equally in right of payment to all our other senior unsecured debt. The senior indenture does not limit the amount of senior debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

Existing Debt

As of March 8, 2012 the Company had no existing subordinated debt and no secured debt.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of common stock, preferred stock or debt securities. Warrants may be offered independently or together with common stock, preferred stock or debt securities offered by any prospectus supplement and may be attached to or separate from those securities. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe in particular the terms of any series of warrants that we may offer in more detail in the applicable prospectus supplement and any related free writing prospectus. The terms of any warrants offered under a prospectus supplement may differ from the terms described below.

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 agreement, which may include a form of warrant certificate, that describes the terms of the of the particular series of warrants we may offer before the issuance of the related series of warrants. We may issue the warrants under a warrant agreement that we will enter into with a warrant agent to be selected by us. The warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation or relationship of agency or trust for or with any registered holders of warrants or beneficial owners of warrants. The following summary of material provisions of the warrants and warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

the title of such warrants;

the aggregate number of such warrants;

the price or prices at which such warrants will be issued;

the currency or currencies (including composite currencies) in which the price of such warrants may be payable;

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

the terms of the securities purchasable upon exercise of such warrants and the procedures and conditions relating to the exercise of such warrants;

the price at which the securities purchasable upon exercise of such warrants may be purchased;

the date on which the right to exercise such warrants will commence and the date on which such right shall expire;

any provisions for adjustment of the number or amount of securities receivable upon exercise of the warrants or the exercise price of the warrants;

if applicable, the minimum or maximum amount of such warrants that may be exercised at any one time;

Table of Contents

if applicable, the designation and terms of the securities with which such warrants are issued and the number of such warrants issued with each such security;

if applicable, the date on and after which such warrants and the related securities will be separately transferable;

information with respect to book-entry procedures, if any;

the terms of any rights to redeem or call the warrants;

United States federal income tax consequences of holding or exercising the warrants, if material; and

any other terms of such warrants, including terms, procedures and limitations relating to the exchange or exercise of such warrants.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

We will specify the place or places where, and the manner in which, warrants may be exercised in the warrant agreement or warrant certificate and applicable prospectus supplement. Upon receipt of payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will, as soon as practicable, issue and deliver the purchased securities. If less than all of the warrants represented by the warrant certificate are exercised, a new warrant certificate will be issued for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Prior to the exercise of any warrants to purchase common stock, preferred stock or debt securities, holders of the warrants will not have any of the rights of holders of the common stock, preferred stock or debt securities purchasable upon exercise, including (i) in the case of warrants for the purchase of common stock or preferred stock, the right to vote or to receive any payments of dividends or payments upon our liquidation, dissolution or winding up on the common stock or preferred stock purchasable upon exercise, if any; or (ii) in the case of warrants for the purchase of debt securities, the right to receive payments of principal of, any premium or interest on the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture.

DESCRIPTION OF UNITS

The following description, together with the additional information we may include in any applicable prospectus supplement, summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement and any related free writing prospectus. The terms of any units offered under a prospectus supplement may differ from the terms described below. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

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 we file with the SEC, the form of unit agreement that describes the terms of the series of units we offer under this prospectus, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

We may issue units comprised of one or more debt securities, shares of common stock, shares of preferred stock and warrants in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units, including, but not limited to:

the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;

Table of Contents

any provisions of the governing unit agreement that differ from those described below; and

any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those described under Description of Common Stock and Preferred Stock, Description of Debt Securities and Description of Warrants will apply to each unit and to any common stock, preferred stock, debt security or warrant included in each unit, respectively.

Issuance in Series

We may issue units in such amounts and in numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

We, the unit agents and any of their agents may treat the registered holder of any unit certificate as an absolute owner of the units evidenced by that certificate for any purpose and as the person entitled to exercise the rights attaching to the units so requested, despite any notice to the contrary.

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee or depositary or warrant agent maintain for this purpose as the holders of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as indirect holders of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Global securities will be registered in the name of the depositary. Consequently, for global securities, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a global security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not legal holders, of the securities.

Table of Contents

Street Name Holders

We may terminate a global security or issue securities that are not issued in global form. In these cases, investors may choose to hold their securities in their own names or in street name. Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we or any applicable trustee or depository will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we or any such trustee or depository will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not legal holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee or third party employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the legal holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with its participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the legal holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of an indenture, or for other purposes. In such an event, we would seek approval only from the legal holders, and not the indirect holders, of the securities. Whether and how the legal holders contact the indirect holders is up to the legal holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form because the securities are represented by one or more global securities or in street name, you should check with your own institution to find out:

how it handles securities payments and notices;

whether it imposes fees or charges;

how it would handle a request for the legal holders' consent, if ever required;

whether and how you can instruct it to send you securities registered in your own name so you can be a legal holder, if that is permitted in the future;

how it would exercise rights under the securities if there were a default or other event triggering the need for legal holders to act to protect their interests; and

if the securities are in book-entry form, how the depository's rules and procedures will affect these matters.

Global Securities

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

A global security is a security that represents one or any other number of individual securities held by a depository. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we issue to, deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depository. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depository for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depository, its nominee or a successor depository, unless special termination situations arise. We describe those situations below under **Special Situations When A Global Security Will Be Terminated**. As a result of these arrangements, the depository, or its nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depository or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

Table of Contents

If the prospectus supplement for a particular security indicates that the security will be issued as a global security, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations For Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only as global securities, an investor should be aware of the following:

an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;

an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;

an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

an investor may not be able to pledge his or her interest in the global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;

the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in the global security. We and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in the global security. We and the trustee also do not supervise the depositary in any way;

the depositary may, and we understand that DTC will, require that those who purchase and sell interests in the global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and

financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in the global security, may also have their own policies affecting payments, notices and other matters relating to the securities. There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, a global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own names, so that they will be direct holders. We have described the rights of holders and street name investors above.

A global security will terminate when the following special situations occur:

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

if the depository notifies us that it is unwilling, unable or no longer qualified to continue as depository for that global security and we do not appoint another institution to act as depository within 90 days;

if we notify any applicable trustee that we wish to terminate that global security; or

if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depository, and neither we nor any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

Table of Contents

PLAN OF DISTRIBUTION

We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

the name or names of any agents or underwriters;

the purchase price of the securities being offered and the proceeds we will receive from the sale;

any over-allotment options under which underwriters may purchase additional securities from us;

any agency fees or underwriting discounts and/or commissions and other items constituting agents' or underwriters' compensation;

any public offering price;

any discounts or concessions allowed or reallocated or paid to dealers; and

any securities exchanges or markets on which such securities may be listed.

We may distribute the securities from time to time in one or more transactions at:

fixed price or prices, which may be changed from time to time;

market prices prevailing at the time of sale;

prices related to such prevailing market prices; or

negotiated prices.

Agents

We may designate agents who agree to use their reasonable efforts to solicit purchases of our securities for the period of their appointment or to sell our securities on a continuing basis. We will name any agent involved in the offering and sale of securities and we will describe any fees or commissions we will pay the agent in the applicable prospectus supplement.

Underwriters

If we use underwriters for a sale of securities, the underwriters will acquire the securities for their own account. The underwriters may resell the securities in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. Subject to certain conditions, the underwriters will be obligated to purchase all the securities of the series offered if they purchase any of the securities of that series. We may change from time to time any public offering price and any discounts or concessions the underwriters allow or reallow or pay to dealers. We may use underwriters with whom we have a material relationship. We will describe the nature of any such relationship in any applicable prospectus supplement naming any such underwriter. Only underwriters we name in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to offerings under this prospectus, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities.

Direct Sales

We may also sell securities directly to one or more purchasers without using underwriters or agents. Underwriters, dealers and agents that participate in the distribution of the securities may be underwriters as defined in the Securities Act, and any discounts or commissions they receive from us and any profit on their resale of the securities may be treated as underwriting discounts and commissions under the Securities Act. We will identify in the applicable prospectus supplement any underwriters, dealers or agents and will describe their compensation. We may have agreements with the underwriters, dealers and agents to indemnify them against specified civil liabilities, including liabilities under the Securities Act. Underwriters, dealers and agents may engage in transactions with or perform services for us in the ordinary course of their businesses.

Table of Contents

Trading Markets and Listing of Securities

Unless otherwise specified in the applicable prospectus supplement, each class or series of securities will be a new issue with no established trading market, other than our common stock, which is currently listed on the NYSE Amex. We may elect to list any other class or series of securities on any exchange or market, but we are not obligated to do so. It is possible that one or more underwriters may make a market in a class or series of securities, but the underwriters will not be obligated to do so and may discontinue any market making at any time without notice. We cannot give any assurance as to the liquidity of the trading market for any of the securities.

Stabilization Activities

Any underwriter may engage in overallocation, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallocation involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of these activities at any time.

Passive Market Making

Any underwriters who are qualified market makers on the NYSE Amex may engage in passive market making transactions in the securities on the NYSE Amex in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security. If all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

Compensation Cap

In compliance with the guidelines of the Financial Regulatory Authority, or FINRA, the maximum aggregate value of all compensation to be received by any FINRA member or independent broker-dealer will not exceed 8% of the gross proceeds from the sale of securities pursuant to this prospectus and any applicable prospectus supplement.

Table of Contents

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon for us by DLA Piper LLP (US), San Diego, California. If the validity of any securities is also passed upon by counsel any underwriters, dealers or agents, that counsel will be named in the prospectus supplement relating to that specific offering.

EXPERTS

The consolidated financial statements as of December 31, 2011 and for the year ended December 31, 2011 and cumulatively for the period from January 1, 2011 to December 31, 2011 and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) as of December 31, 2011 incorporated in this prospectus by reference to the annual report on Form 10-K for the year ended December 31, 2011 have been incorporated in reliance upon the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of such firm as an expert in accounting and auditing.

The consolidated balance sheet of ADVENTRX Pharmaceuticals, Inc. and its subsidiaries as of December 31, 2010, and the related consolidated statements of operations, stockholders' equity (deficit) and comprehensive loss and cash flows for the year then ended and for the period from January 1, 2002 through December 31, 2010 are incorporated by reference herein and in the registration statement in reliance upon the report of J.H. Cohn LLP, an independent registered public accounting firm, given on the authority of such firm as an expert in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information electronically with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. You can request copies of these documents by writing to the SEC and paying a fee for the copying costs. The SEC also maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including us. The SEC's Internet site can be found at <http://www.sec.gov>. In addition, we make available on or through our Internet site copies of these reports as soon as reasonably practicable after we electronically file or furnish them to the SEC. Our Internet site can be found at <http://www.adventrx.com>.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

We are allowed to incorporate by reference information contained in documents that we file with the SEC. This means that we can disclose important information to you by referring you to those documents and that the information in this prospectus is not complete. You should read the information incorporated by reference for more detail. We incorporate by reference in two ways. First, we list below certain documents that we have already filed with the SEC. The information in these documents is considered part of this prospectus. Second, the information in documents that we file in the future will update and supersede the information currently in, and be incorporated by reference in, this prospectus.

We incorporate by reference into this prospectus the documents listed below, any filings we make with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the initial registration statement of which this prospectus is a part and prior to the effectiveness of the registration statement, and any filings we make with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act from the date of this prospectus until the termination of this offering (in each case, except for the information furnished under Item 2.02 or Item 7.01 in any current report on Form 8-K and Form 8-K/A):

our annual report on Form 10-K for the year ended December 31, 2011 filed with the SEC on March 8, 2012;

our current reports on Form 8-K filed with the SEC on January 23, 2012 (File No. 001-32157-12539625), February 27, 2012 (File No. 001-32157-12642097) and March 8, 2012; 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. 001-32157-041020580).

Table of Contents

We will provide each person, including any beneficial owner, to whom a prospectus is delivered, a copy of any or all of the information that has been incorporated by reference into this prospectus but not delivered with this prospectus upon written or oral request at no cost to the requester. Requests should be directed to: ADVENTRX Pharmaceuticals, Inc., 12390 El Camino Real, Suite 150, San Diego, CA 92130, Attn: Investor Relations, telephone: (858) 552-0866.

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC. That registration statement contains more information than this prospectus regarding us and our common stock, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's Internet website.

You should rely only on the information provided in and incorporated by reference into this prospectus or any prospectus supplement. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front cover of these documents.

Table of Contents

\$30,000,000

Common Stock

Prospectus Supplement

Cowen and Company

February 10, 2014