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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-219794

Prospectus supplement
(to Prospectus dated August 18, 2017)

Up to \$50,000,000 maximum aggregate offering price of Common Stock



We have entered into a sales agreement with J.P. Morgan Securities LLC, Cantor Fitzgerald & Co. and Ladenburg Thalmann & Co. Inc. (which we refer to collectively as the "Sales Agents," and each individually as a "Sales Agent"), relating to shares of our common stock offered by this 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 \$50,000,000 from time to time through any of the sales agent.

Our common stock is traded on the NASDAQ Capital Market under the symbol "STML." On March 15, 2018, the per share closing price of our common stock as reported on the NASDAQ Capital Market was \$15.00 per share.

Sales of our common stock, if any, under this prospectus may be made in sales deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Subject to the terms of the sales agreement, J.P. Morgan Securities LLC, Cantor Fitzgerald & Co. and Ladenburg Thalmann & Co. Inc. will act as sales agents and use commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with their normal trading and sales practices, on mutually agreed terms between the Sales Agents and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Under the Distribution Agreement, we may also sell shares of common stock to a Sales Agent, as principal for its own account, at a price to be agreed upon at the time of sale. If we sell shares to a Sales Agent as principal, we will enter into a separate terms agreement with such Sales Agent, and we will describe the agreement in a separate prospectus supplement or pricing supplement.

Each Sales Agents will be entitled to compensation at a commission rate of 3% of the gross sales price per share sold under the sales agreement. In connection with the sale of shares of our common stock on our behalf, each Sales Agent will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of each Sales Agent will be deemed to be underwriting commissions or discounts.

Investing in our securities involves certain risks. See "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2017, which has been filed with the Securities and Exchange Commission and are incorporated by reference into this prospectus. You should read the entire prospectus carefully before you make your investment decision.

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.

J.P. Morgan

Cantor

Ladenburg Thalmann

Prospectus Supplement dated March 16, 2018

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About this prospectus supplement

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus, dated August 18, 2017, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus supplement, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference that was filed with the U.S. Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, you should rely on the information in this prospectus supplement; 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 the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

This prospectus relates to part of a registration statement that we have filed with the Securities and Exchange Commission, or SEC, utilizing a "shelf" registration process. The \$50,000,000 of common stock that may be offered, issued and sold under this prospectus is included in the \$175,000,000 of securities that may be offered, issued and sold by us pursuant to our shelf registration statement. This prospectus is deemed a prospectus supplement to the base prospectus included in the registration statement of which this prospectus forms a part.

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 herein 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.

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 accompanying prospectus 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 and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do 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 and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless otherwise stated, all references in this prospectus supplement to "we," "us," "our," "Stemline," the "Company" and similar designations refer to Stemline Therapeutics, Inc. This prospectus supplement contains trademarks and trade names of Stemline Therapeutics, Inc., including our name and logo. Other service marks, trademarks and trade names referred to in this document are the property of their respective owners.

Special cautionary notice regarding forward-looking statements

Certain matters discussed in this prospectus supplement and the accompanying prospectus, including matters discussed under the captions "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K, each as incorporated by reference herein, may constitute forward-looking statements for purposes of the Securities Act of 1933, as amended, or the Securities Act, and the Securities Exchange Act of 1934, as amended, or the Exchange Act, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from the future results, performance or achievements expressed or implied by such forward-looking statements. The words "anticipate," "believe," "estimate," "may," "expect" and similar expressions are generally intended to identify forward-looking statements. Our actual results may differ materially from the results anticipated in these forward-looking statements due to a variety of factors, including, without limitation, those discussed under the captions "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this prospectus supplement and the documents incorporated by reference herein, as well as other factors which may be identified from time to time in our other filings with the SEC, or in the documents where such forward-looking statements appear. All written or oral forward-looking statements attributable to us are expressly qualified in their entirety by these cautionary statements.

Some of the factors that we believe could cause actual results to differ from those anticipated or predicted include:

- the success and timing of our clinical trials, including safety and efficacy of our product candidates, patient accrual, unexpected or expected safety events, and the usability of data generated from our trials;
- our ability to successfully file and obtain timely marketing approval from the U.S. Food and Drug Administration, or FDA, or comparable foreign regulatory agency for one or more Biologics License Applications, or BLAs, or New Drug Applications, or NDAs;
- our ability to obtain and maintain marketing approval from regulatory agencies for our products in the U.S. and foreign countries;
- our ability to adhere to ongoing compliance requirements of all health authorities, in the U.S. and foreign countries;
- our ability to obtain and maintain adequate reimbursement for our products;
- our ability to obtain the desired labeling of our products under any regulatory approval we might receive;
- our plans to develop and commercialize our products;
- the successful development and implementation of sales and marketing campaigns;
- the loss of key scientific or management personnel;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- our ability to successfully compete in the potential markets for our product candidates, if commercialized;

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- regulatory developments in the United States and foreign countries;
- the rate and degree of market acceptance of any of our product candidates;
- new products, product candidates or new uses for existing products or technologies introduced or announced by our competitors and the timing of these introductions or announcements;
- market conditions in the pharmaceutical and biotechnology sectors;
- our available cash and investments;
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- our ability to obtain additional funding;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- our ability to maintain the license agreements for SL-401, SL-801, SL-701 and our other in-licensed product candidates;
- the success and timing of our preclinical studies, including those intended to support an Investigational New Drug, or IND, application;
- the ability of our product candidates to successfully perform and advance in clinical trials;
- our ability to obtain and maintain authorization from regulatory authorities for use of our product candidates for initiation and conduct of clinical trials;
- our ability to manufacture and supply our products, gain access to products we plan to use in combination studies and the performance of and reliance on third-party manufacturers and suppliers;
- the performance of our clinical research organizations, clinical trial sponsors, and clinical trial investigators; and
- our ability to successfully implement our strategy.

The forward-looking statements contained in this prospectus supplement and accompanying prospectus reflect our views and assumptions only as of the date of this prospectus supplement. Except as required by law, we assume no responsibility for updating any forward-looking statements.

We qualify all of our forward-looking statements by these cautionary statements. In addition, with respect to all of our forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

Prospectus supplement summary

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the information referred to in the section entitled "Risk Factors" beginning on page S-8 of this prospectus supplement, as well as the other documents that we incorporate by reference into this prospectus supplement and the accompanying base prospectus, including our financial statements and the exhibits to the registration statement of which this prospectus supplement and the accompanying base prospectus is a part.

Overview

We are a clinical stage biopharmaceutical company focused on discovering, acquiring, developing and potentially commercializing innovative oncology therapeutics that target difficult to treat cancers. Our clinical pipeline includes: SL-401, SL-801, and SL-701.

SL-401

SL-401 is a novel targeted therapy directed to the interleukin-3 receptor- α , or CD123, a target expressed on a wide range of malignancies. SL-401 has completed a pivotal Phase 2 trial in patients with blastic plasmacytoid dendritic cell neoplasm, or BPDCN. SL-401 is also being assessed in additional indications including Phase 1/2 trials in patients with high-risk myeloproliferative neoplasms, or MPNs, focused on chronic myelomonocytic leukemia, or CMML and Myelofibrosis or MF, and patients with acute myeloid leukemia, or AML, and in combination with other agents in a Phase 1 trial in patients with relapsed/refractory multiple myeloma. In August 2016, SL-401 was granted Breakthrough Therapy Designation, or BTB, from the U.S. Food and Drug Administration, or FDA, for the treatment of BPDCN.

On October 31, 2017, we announced that the pivotal Phase 2 trial of SL-401 in BPDCN met its primary endpoint. The pivotal Phase 2 trial in BPDCN is an open label, non-randomized, single arm clinical trial. We believe this trial is the largest multicenter prospective study ever conducted in BPDCN. The trial enrolled 45 BPDCN (32 first line, 13 relapsed/refractory) patients and consisted of 3 Stages: Stage 1 (lead-in, dose escalation), Stage 2 (expansion), and Stage 3 (pivotal, confirmatory). To ensure ongoing patient access to SL-401, we are currently enrolling both first-line and relapsed/refractory BPDCN patients in an additional cohort, Stage 4. We believe the results of this trial could support marketing approval and we plan to include such results as part of a Biologics License Application, or BLA, that seeks U.S. marketing approval. We anticipate such a filing could be completed in the first half of 2018. If successful, we project marketing approval could be attained in the second half of 2018, or soon thereafter. Later this year, we anticipate feedback from the European Medicines Agency, or EMA, regarding a potential regulatory filing.

SL-801

SL-801 is a structurally novel, oral, small molecule, reversible inhibitor of Exportin-1, or XPO1, a nuclear transport protein implicated in a variety of malignancies. SL-801 has demonstrated preclinical in vitro and in vivo antitumor activity against a wide array of solid and hematologic cancers. SL-801's potential ability to reversibly bind XPO1 may offer the possibility to mitigate side effects and help optimize the therapeutic index. We are currently enrolling patients with advanced solid tumors in a Phase 1 dose escalation trial of single agent SL-801.

SL-701

SL-701 is an immunotherapy designed to direct the immune system to attack targets present on certain malignancies, including brain cancer. SL-701 is comprised of 3 short synthetic peptides that correspond to epitopes of targets including IL-13R α 2, EphA2, and survivin, present on brain cancer. We advanced SL-701 into a corporate sponsored Phase 2 trial in adult patients with second-line glioblastoma. In Stage 1 of this trial, SL-701 was administered as a single agent with the immunostimulants GM-CSF and Imiquimod. In Stage 2 of the trial, SL-701 was administered, with the immunostimulant poly-ICLC in combination with bevacizumab. Both stages of the trial have completed dosing and patients are being followed for outcomes including survival.

General

We have devoted substantially all of our resources to develop our product candidates, manufacture our product candidates, prepare for commercialization, build our intellectual property portfolio, execute our business plan, raise capital, and provide general and administrative support for these operations. We have generated minimal revenues to date, have not generated any revenue from product sales, and have funded our operations primarily through public and private sales of common stock and private sales of convertible preferred stock to our investors.

Company information

We were incorporated under the laws of the State of Delaware in August 2003. Our principal executive office is located at 750 Lexington Avenue, Eleventh Floor, New York, New York 10022 and our telephone number is (646) 502-2311.

Our website address is www.stemline.com. We are not including the information on our website as a part of, nor incorporating it by reference into, this prospectus supplement.

The offering

Common stock offered by us	Shares of our common stock, par value \$0.0001, having an aggregate offering price of up to \$50 million.
Common stock to be outstanding after the offering	25,313,595 shares of our common stock on the NASDAQ Capital Market are outstanding as of December 31, 2017. The actual number of shares issued in connection with this offering will vary depending on how many shares of our common stock we choose to sell and the prices at which such sales occur.
Manner of offering	Sales of shares of our common stock under this prospectus supplement may be made by any method deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended. Subject to the terms of the sales agreement, each Sales Agent will make all sales using commercially reasonable efforts consistent with their normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of The NASDAQ Capital Market, on mutually agreeable terms between the Sales Agent and us. See "Plan of Distribution" beginning on page S-12 of this prospectus supplement.
Commercially reasonable efforts	No Sales Agent is required to sell any specific number or dollar amount of our common stock, but each Sales Agent has agreed to make all sales using commercially reasonable efforts consistent with such Sales Agent's normal trading and sales practices. See "Plan of Distribution" in this prospectus supplement.
Use of proceeds	We intend to use the net proceeds from this offering for (i) clinical, regulatory, manufacturing and, if and when approved, potential commercial activities of SL-401; (ii) clinical development of SL-801 and SL-701; (iii) research and development activities; (iv) potential acquisitions and in-licensing; and (v) other general corporate purposes. See "Use of Proceeds" on page S-9 of this prospectus supplement.
Risk factors	See "Risk Factors" beginning on page S-8 and our "Risk Factors" beginning on page 30 of our Annual Report on Form 10-K for the year ended December 31, 2017, which is incorporated by reference herein, for a discussion of factors that you should consider before investing in our common stock.
NASDAQ Capital Market symbol	STML

The number of shares of our common stock outstanding after this offering is based on 25,313,595 actual shares of our common stock outstanding as of December 31, 2017, and excludes, as of such date:

- 3,174,964 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2017, at a weighted-average exercise price of \$8.74 per share, of which 1,912,882 shares were vested as of such date;
- 99,529 shares of common stock issuable upon the exercise of warrants outstanding as of December 31, 2017, at an exercise price of \$15.00 per share; and
- 1,089,975 shares of our common stock available for future issuance under our 2016 Equity Incentive Plan, or the 2016 Equity Plan, as of December 31, 2017.

Unless otherwise indicated, all information in this prospectus supplement assumes:

- no exercise of the outstanding options or warrants.

Risk factors

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks discussed below, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference including the section "Risk Factors" beginning on page 30 of our Annual Report on Form 10-K for the year ended December 31, 2017, which is incorporated by reference herein, and in any free writing prospectus that we have authorized for use in connection with this offering. The risks described below may not be the only ones relating to our company. Additional risks that we currently believe are immaterial or risks not currently known to us may also impair our business and operations. Our business, results of operation, financial condition, cash flow and prospects and the trading price of our common stock could be harmed as a result of any of these risks, and investors may lose all or part of their investment.

Risks associated with this offering

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We will likely seek to raise additional capital through a combination of private and public equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of existing stockholders will be diluted, and the terms may include liquidation or other preferences that adversely affect stockholder rights. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third-parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We have broad discretion over the use of our cash, cash equivalents and marketable securities, including the net proceeds we receive in this offering, and may not use them effectively.

Our management has broad discretion to use our cash, cash equivalents and marketable securities, including the net proceeds we receive in this offering, to fund our operations and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use to fund operations, we may invest our cash, cash equivalents and marketable securities in a manner that does not produce income or that loses value.

We do not expect to pay dividends on our capital stock in the foreseeable future.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business, and we do not anticipate paying any cash dividends on our capital stock in the foreseeable future. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Use of proceeds

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$50 million from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time.

We expect to use the net proceeds from this offering to fund our continued research and development initiatives in connection with expanding our product pipeline and for other general corporate purposes.

We may also use a portion of the net proceeds to acquire or invest in complementary businesses, products and technologies. Although we currently have no specific agreements, commitments or understandings with respect to any acquisition or investment, we evaluate acquisition and investment opportunities and may engage in related discussions with other companies from time to time.

The timing and amounts of our actual expenditures will depend on several factors, including data results, progression of our clinical development programs as well as our joint collaborators. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from an offering. Accordingly, our management will have broad discretion in the application of proceeds. Pending the uses described above, we will invest the net proceeds in short-term and long-term, investment grade, interest-bearing securities.

Price range of common stock

Our common stock is listed on The NASDAQ Capital Market under the symbol "STML" and has been publicly traded since January 29, 2013. Prior to that time, there was no public market for our common stock. As a result, we have not set forth quarterly information with respect to the high and low sales prices for our common stock for such period.

As of March 15, 2018, the last sale price of our common stock was \$15.00 per share, as reported by The NASDAQ Capital Market. There were approximately 137 holders of record of our common stock as of that date. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

The following table sets forth the ranges of high and low sales price per share of our common stock as reported on The NASDAQ Capital Market for the period indicated.

	High	Low
2015		
First Quarter	18.94	12.77
Second Quarter	17.02	11.38
Third Quarter	13.24	8.31
Fourth Quarter	9.92	5.88
2016		
First Quarter	6.50	3.88
Second Quarter	9.66	4.62
Third Quarter	11.29	6.40
Fourth Quarter	14.60	10.08
2017		
First Quarter	14.25	10.45
Second Quarter	9.65	7.30
Third Quarter	11.70	7.30
Fourth Quarter	16.00	10.20
2018		
First Quarter (through March 15, 2018)	18.75	13.05

Dividend policy

We have never declared or paid any cash dividends on our common stock and do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors.

Plan of distribution

We have entered into a Distribution Agreement (which we refer to as the "Distribution Agreement") with J.P. Morgan Securities LLC, Cantor Fitzgerald & Co. and Ladenburg Thalmann & Co. Inc. (which we refer to collectively as the "Sales Agents," and each individually as a "Sales Agent"), under which we may issue and sell from time to time shares of our common stock having an aggregate gross offering price of up to \$50 million through any of the Sales Agents. Sales of our common stock, if any, may be made in transactions that are deemed to be "at the market offerings," as defined in Rule 415(a)(4) promulgated under the Securities Act, including sales made by means of ordinary brokers' transactions on the Nasdaq Global Select Market at market prices.

Each Sales Agent will offer our common stock subject to the terms and conditions of the Distribution Agreement on a daily basis or otherwise as agreed upon by us and such Sales Agent. We will designate the maximum amount of our common stock to be sold through a Sales Agent on a daily basis or otherwise determine such maximum amount together with such Sales Agent. Subject to the terms and conditions of the Distribution Agreement, each Sales Agent will use its commercially reasonable efforts to sell on our behalf the common stock we designate from time to time. We may instruct the Sales Agents not to sell our common stock if the sales cannot be effected at or above the price designated by us in any such instruction. No Sales Agent will be obligated to use its reasonable efforts to sell our common stock at any price below the designated price. We or the Sales Agents may suspend the offering of our common stock under the Distribution Agreement upon proper notice and subject to other conditions.

Each Sales Agent will receive from us a commission of up to 3% of the gross sales price per share of our common stock for any shares sold through such Sales Agent under the Distribution 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 shares. We have agreed to pay for certain of the Sales Agents' expenses in certain circumstances.

Each Sales Agent will provide written confirmation to us following the close of trading on the Nasdaq Global Select Market each day on which shares of our common stock are sold by such Sales Agent for us under the Distribution Agreement. Each confirmation will include the number of shares sold on that day, the gross sales price per share and the net proceeds to us.

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

Under the terms of the Distribution Agreement, we also may sell our common stock to a Sales Agent as principal for its own account, at a price agreed upon at the time of sale. If we sell shares to a Sales Agent as principal, we will enter into a separate terms agreement with such Sales Agent, and we will describe such agreement in a separate prospectus supplement or pricing supplement.

We will report in a prospectus supplement and/or our filings with the SEC under the Exchange Act at least quarterly the number of shares of our common stock sold through the Sales Agents under the Distribution Agreement, the net proceeds to us and the compensation paid by us to the Sales Agents in connection with the sales of our common stock.

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In connection with the sale of our common stock on our behalf, a Sales Agent may be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation paid to such Sales Agent may be deemed to be underwriting commissions or discounts. We have agreed in the Distribution Agreement to provide indemnification and contribution to the Sales Agents against certain civil liabilities, including liabilities under the Securities Act.

Each Sales Agent and its respective affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the Sales Agents and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The Sales Agents and their respective affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

If either any Sales Agent or we have reason to believe that the exemptive provisions set forth in Rule 101(c)(1) of Regulation M under the Exchange Act are not satisfied, that party will promptly notify the other and sales of our common stock under the Distribution Agreement will be suspended until that or other exemptive provisions have been satisfied in the judgment of such Sales Agent and us.

The offering of our common stock pursuant to the Distribution Agreement will terminate upon the earlier of (i) the sale of all shares of our common stock subject to the Distribution Agreement and (ii) the termination of the Distribution Agreement by us and/or by the Sales Agents.

We estimate that the total expenses of the offering payable by us, excluding discounts and commissions and other amounts payable to the Sales Agents under the Distribution Agreement, will be approximately \$100,000. We have also agreed in certain circumstances to pay for the reasonable fees and disbursements of the Sales Agents in connection with the offering.

Legal matters

The validity of the common stock offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Alston & Bird LLP, New York, New York. The Sales Agents have been represented by Davis Polk & Wardwell LLP, New York, New York.

Experts

The financial statements of Stemline Therapeutics, Inc. included in Stemline Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2017 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

Where you can find more information

We file reports with the SEC on an annual basis using Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K. You may read and copy any such reports and amendments thereto 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 information on the operation of the Public Reference Room. Additionally, the SEC maintains a website that contains annual, quarterly and current reports, proxy statements, and other information that issuers (including us) file electronically with the SEC. The SEC's website address is <http://www.sec.gov>. You can also obtain copies of materials we file with the SEC from our Internet website found at www.stemline.com. Our stock is quoted on The Nasdaq Capital Market under the symbol "STML."

Incorporation of certain information by reference

The SEC allows us to "incorporate by reference" information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Information contained in this prospectus supplement and the accompanying prospectus, and information that we file with the SEC in the future and incorporate by reference in this prospectus supplement and the accompanying prospectus, will automatically update and supersede this information. We incorporate by reference in this prospectus supplement and the accompanying prospectus the documents listed below, any future documents we file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement and until the completion or termination of this offering (in each case, except for the information in any of the foregoing Current Reports on Form 8-K furnished under Item 2.02 or Item 7.01 thereof):

- (a) Our Annual Report on Form 10-K for the year ended December 31, 2017;
- (b) The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2016 from our definitive proxy statement on Schedule 14A filed on May 1, 2017; and
- (c) Description of our common stock, which is contained in the Registration Statement on Form 8-A, as filed with the SEC on July 30, 2012, as supplemented by the Description of Common Stock found on page 5 of the accompanying prospectus and including any amendments or reports filed for the purpose of updating such description.

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A statement contained in a document incorporated by reference into this prospectus supplement and the accompanying prospectus shall be deemed to be modified or superseded for purposes of this prospectus supplement and the accompanying prospectus to the extent that a statement contained in this prospectus supplement, the accompanying prospectus, or in any other subsequently filed document which is also incorporated in this prospectus supplement and the accompanying prospectus modifies or replaces such statement. Any statements so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement and the accompanying prospectus.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting: Stemline Therapeutics, Inc., 750 Lexington Avenue, Eleventh Floor, New York, NY 10022, (646) 502-2311, email address: info@stemline.com. In addition, copies of any or all of the documents incorporated herein by reference may be accessed at our website at www.stemline.com. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus.

You should rely only on information contained in, or incorporated by reference into, this prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus supplement or incorporated by reference in this prospectus supplement.

PROSPECTUS

\$175,000,000

Stemline Therapeutics, Inc.

**Common Stock
Preferred Stock
Warrants
Debt Securities
Units**

The following are types of securities that we may offer, issue and sell from time to time, together or separately:

- shares of our common stock;
- shares of our preferred stock;
- warrants;
- debt securities; and
- units consisting of any combination of our common stock, preferred stock, warrants or debt securities.

We may offer these securities in amounts, at prices, and on terms determined at the time of offering. We may sell these securities directly to you through agents we select or through underwriters and dealers we select. If we use agents, underwriters or dealers to sell these securities, we will name them and describe their compensation in a prospectus supplement. You should read this prospectus and any prospectus supplement carefully before you invest.

This prospectus provides a general description of the securities we may offer. Each time we sell securities, we will provide specific terms of the securities offered in a supplement to this prospectus. The prospectus supplement may also add, update or change information contained in this prospectus. You should read this prospectus and the applicable prospectus supplement carefully, together with additional information described under the heading "Where You Can Find More Information," before you invest in any securities. This prospectus may not be used to consummate a sale of securities unless accompanied by the applicable prospectus supplement.

Our common stock is traded on the Nasdaq Capital Market under the symbol "STML." On August 7, 2017, the per share closing price of our common stock as reported on the Nasdaq Capital Market was \$8.85 per share.

Investing in our securities involves certain risks. See "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2016, as well as our Quarterly Reports on Form 10-Q for the periods ended March 31, 2017 and June 30, 2017, which have been filed with the SEC and are incorporated by reference into this prospectus. You should read the entire prospectus carefully before you make your investment decision.

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 August 18, 2017.

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STEMLINE THERAPEUTICS, INC.

Overview

We are a clinical stage biopharmaceutical company focused on discovering, acquiring, developing and potentially commercializing innovative oncology therapeutics that target difficult to treat cancers. We are currently developing three clinical stage product candidates: SL-401, SL-801, and SL-701.

SL-401

SL-401 is a targeted therapy directed to the interleukin-3 receptor, or IL-3R (CD123), present on a wide range of hematologic cancers. SL-401 is being advanced through a pivotal Phase 2 trial in patients with blastic plasmacytoid dendritic cell neoplasm, or BPDCN. SL-401 is also being assessed in additional indications including in Phase 1/2 trials of patients with myeloproliferative neoplasms, or MPNs, focused on chronic myelomonocytic leukemia, or CMML, and myelofibrosis; acute myeloid leukemia, or AML, in complete remission with minimal residual disease, or MRD; and in combination with other agents in relapsed/refractory multiple myeloma. Factors that may impact next steps for SL-401 in these additional indications include enrollment trends, safety and efficacy results, regulatory and other considerations.

SL-401 was granted Breakthrough Therapy Designation, or BTM, by the U.S. Food and Drug Administration, or FDA, for BPDCN in August 2016. The FDA awarded Orphan Drug status to SL-401 for the treatment of AML in February 2011 and for BPDCN in June 2013. The European Medicines Agency, or EMA, awarded Orphan Drug status to SL-401 for the treatment of AML in October 2015 and for BPDCN in November 2015.

In the second half of 2017, we plan to announce results from the pivotal Phase 2 trial of SL-401 in BPDCN, including data from the Stage 3 cohort. If, in our view, the results of this trial could support pursuing marketing approval, which it may not, we plan to include such results as part of a Biologics License Application, or BLA, that seeks U.S. marketing approval, and we anticipate such a filing could begin in the fourth quarter of 2017 or first quarter of 2018.

SL-801

SL-801 is a structurally novel, oral, small molecule, reversible inhibitor of Exportin-1, or XPO1, a tumor-promoting nuclear transport protein. SL-801 has demonstrated potent preclinical in vitro and in vivo antitumor activity against a wide array of solid and hematologic cancers. SL-801's potential ability to reversibly bind XPO1 may offer the possibility to mitigate side effects and help optimize the therapeutic index. We are currently enrolling patients with advanced solid tumors in a Phase 1 dose escalation trial of single agent SL-801. We have completed five dose levels, and are currently enrolling patients in the sixth dosing cohort. We plan to provide an update on this Phase 1 trial at a medical conference later this year.

SL-701

SL-701 is an immunotherapy designed to direct the immune system to attack targets present on brain cancer, and is comprised of several short synthetic peptides that correspond to epitopes of targets including IL-13R α 2, EphA2, and survivin. We conducted a Phase 2 trial of SL-701 in adult patients with second-line glioblastoma, or GBM. In Stage 1 of this trial, SL-701 was administered as a single agent, with the immunostimulants GM-CSF and Imiquimod. In Stage 2 of the trial, SL-701 was administered in combination with bevacizumab, with the immunostimulant poly-ICLC. Both stages of the trial have completed enrollment and dosing and patients are being followed for survival. Survival trends and other data will be considered when deciding next steps for the program. These steps may include conducting larger studies, including randomized studies, further combination studies with novel

agents, (e.g., checkpoint inhibitors), that could be conducted alone or via partnerships; or cessation of the program. If additional studies are conducted, this may entail significant manufacturing campaigns and commitments around SL-701 and certain immunostimulants depending upon the choice and availability of immunostimulants. SL-701 was awarded Orphan Drug designation from the FDA for the treatment of glioma in January 2015.

Our Company

We were incorporated under the laws of the State of Delaware in August 2003. Our principal executive office is located at 750 Lexington Avenue, Eleventh Floor, New York, New York 10022 and our telephone number is (646) 502-2311.

THE OFFERING

Use of proceeds We intend to use the net proceeds of any offering as set forth in the applicable prospectus supplement.

NASDAQ Capital Market symbol STML

FORWARD-LOOKING STATEMENTS

This prospectus includes statements that are, or may be deemed, "forward-looking statements." In some cases, these forward-looking statements can be identified by the use of forward-looking terminology, including the terms "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately" or, in each case, their negative or other variations thereon or comparable terminology, although not all forward-looking statements contain these words. They appear in a number of places throughout this prospectus and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our history of net operating losses and uncertainty regarding our ability to obtain capital and achieve profitability, our ability to develop and commercialize our product candidates, our ability to advance our development programs, enroll our trials, and achieve clinical endpoints, our ability to use or expand our technology to build a pipeline of product candidates, our ability to obtain and maintain regulatory approval of our product candidates and comply with ongoing regulatory requirements, our ability to successfully operate in a competitive industry and gain market acceptance by physician, provider, patient, and payor communities, our reliance on third parties, unstable economic or market conditions, and our ability to obtain and adequately protect intellectual property rights for our product candidates.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics, and healthcare, regulatory and scientific developments and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this prospectus. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this prospectus, they may not be predictive of results or developments in future periods.

WHERE YOU CAN FIND MORE INFORMATION

We file reports with the SEC on an annual basis using Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K. You may read and copy any such reports and amendments thereto 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 information on the operation of the Public Reference Room. Additionally, the SEC maintains a website that contains annual, quarterly, and current reports, proxy statements, and other information that issuers (including us) file electronically with the SEC. The SEC's website address is <http://www.sec.gov>. You can also obtain copies of materials we file with the SEC from our Internet website found at www.stemline.com. Our stock is quoted on the Nasdaq Capital Market under the symbol "STML."

IMPORTANT INFORMATION ABOUT THIS PROSPECTUS

This prospectus is part of a "shelf" registration statement that we filed with the SEC. By using a shelf registration statement, we may sell our securities, as described in this prospectus, from time to time in one or more offerings. We may use the shelf registration statement to offer and sell securities described in this prospectus. Each time we sell securities, we will provide a prospectus supplement to this prospectus that contains specific information about the terms of such offering. The supplement may also add, update or change information contained in this prospectus. Before purchasing any securities, you should carefully read both this prospectus and any supplement, together with the additional information incorporated into this prospectus or described under the heading "Where You Can Find More Information."

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You should rely only on the information contained or incorporated by reference in this prospectus and any prospectus supplement. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We will not make an offer to sell securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus, as well as information we previously filed with the SEC and have incorporated by reference, is accurate as of the date on the front cover of this prospectus only, or when such document was filed with the SEC. Our business, financial condition, results of operations and prospects may have changed since the relevant date.

We will not use this prospectus to offer and sell securities unless it is accompanied by a prospectus supplement that more fully describes the terms of the offering.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with them. This means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this document. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (1) after the date of the initial registration statement, as amended, and prior to effectiveness of the registration statement, and (2) after the date of this prospectus and prior to the termination of this offering. Such information will automatically update and supersede the information contained in this prospectus and the documents listed below; provided, however, that we are not, unless specifically indicated, incorporating any information furnished under Item 2.02 or Item 7.01 of any current report on Form 8-K, whether listed below or filed in the future, or related exhibits furnished pursuant to Item 9.01 of Form 8-K:

- (a) Our Annual Report on Form 10-K for the year ended December 31, 2016;
- (b) Our Quarterly Report on Form 10-Q for the quarters ended March 31, 2017 and June 30, 2017;
- (c) Our Current Reports on Form 8-K filed with the SEC on January 6, 2017, January 20, 2017, March 17, 2017, March 24, 2017, May 11, 2017, June 20, 2017 and August 8, 2017;
- (d) Our Definitive Proxy Statement on Schedule 14A, filed with the SEC on May 1, 2017; and
- (e) Description of our common stock, which is contained in the Registration Statement on Form 8-A, as filed with the SEC on July 30, 2012, as supplemented by the Description of Common Stock found on page 6 of the base prospectus and including any amendments or reports filed for the purpose of updating such description.

We will provide to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, a copy of any or all of the information that we have incorporated by reference into this prospectus. We will provide this information upon written or oral request at no cost to the requester. You may request this information by contacting our corporate headquarters at the following address: 750 Lexington Avenue, Eleventh Floor, New York, New York 10022, Attn: Chief Accounting Officer, or by calling (646) 502-2311.

RATIO OF EARNINGS/ DEFICIENCY TO FIXED CHARGES

The following table sets forth, for each of the periods presented, our ratio of earnings to fixed charges and our coverage deficiency. You should read this table in conjunction with the financial statements and notes incorporated by reference in this prospectus.

(in thousands)	Six Months Ended June 30, 2017	Year Ended December 31, 2016	Year Ended December 31, 2015	Year Ended December 31, 2014	Year Ended December 31, 2013	Year Ended December 31, 2012
Net loss	(30,022,946)	(38,303,005)	(37,243,861)	(28,829,975)	(24,196,511)	(6,274,782)
Ratio of earnings to fixed charges(1)	N/A	N/A	N/A	N/A	N/A	N/A
Coverage deficiency	(30,022,946)	(38,303,005)	(37,243,861)	(28,829,975)	(24,196,511)	(6,274,782)

- (1) We did not record earnings for the six months ended June 30, 2017, and for the years ended December 31, 2016, 2015, 2014, 2013 and 2012. Accordingly, our earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of earnings to fixed charges for such periods.

DESCRIPTION OF SECURITIES WE MAY OFFER

This prospectus contains summary descriptions of the securities we may offer from time to time. These summary descriptions are not meant to be complete descriptions of each security. The particular terms of any security will be described in the related prospectus supplement.

DESCRIPTION OF COMMON STOCK

The following summary of the terms of our common stock may not be complete and is subject to, and qualified in its entirety by reference to, the terms and provisions of our restated certificate of incorporation and our amended and restated by-laws. You should refer to, and read this summary together with, our restated certificate of incorporation and amended and restated by-laws to review all of the terms of our common stock that may be important to you.

Common Stock

Under the terms of our restated certificate of incorporation, we are authorized to issue a total of 53,750,000 shares of common stock, par value \$0.0001 per share. As of August 8, 2017, we had issued and outstanding 25,280,024 shares of our common stock. All outstanding shares of our common stock are fully paid and nonassessable. Our common stock is listed on The Nasdaq Capital Market and trades under the symbol "STML" and has been publicly traded since January 29, 2013. Prior to that time, there was no public market for our common stock.

Holders

The number of record holders of our 25,280,024 shares of outstanding common stock as of August 8, 2017 was 136. This number does not include beneficial owners whose shares are held by nominees in street name.

Dividends

We have never declared or paid any cash dividends on our common stock and do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors.

Voting Rights

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Holders of our common stock are not entitled to vote on any amendment to our restated certificate of incorporation that relates solely to the terms of one or more outstanding series of preferred stock. An election of directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights or other rights of outstanding preferred stock.

Liquidation and Dissolution

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the preferential or other rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption, conversion or similar rights. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Transfer Agent

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Anti-Takeover Provisions

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Staggered board; removal of directors

Our restated certificate of incorporation and our amended and restated by-laws divide our board of directors into three classes with staggered three-year terms. In addition, a director may be removed only for cause and only by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors. Any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. The classification of our board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our Company.

Super-majority voting

The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or by-laws, unless a corporation's certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our amended and restated by-laws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes which all our stockholders would be entitled to cast in an election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described in the prior two paragraphs.

Stockholder action; special meeting of stockholders

Our restated certificate of incorporation provides that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of such stockholders and may not be effected by any consent in writing by such stockholders. Our restated certificate of incorporation and our amended and restated by-laws also provide that, except as otherwise required by law, special meetings of our stockholders can only be called by our chairman of the board, our chief executive officer or our board of directors and business transacted at any special meeting is limited to the stated purposes of the meeting.

Authorized but unissued shares

The authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing standards of The Nasdaq Capital Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

DESCRIPTION OF PREFERRED STOCK

The following summary of the terms of our preferred stock may not be complete and is subject to, and qualified in its entirety by reference to, the terms and provisions of our restated certificate of incorporation and our amended and restated by-laws. You should refer to, and read this summary together with, our restated certificate of incorporation and amended and restated by-laws to review all of the terms of our preferred stock that may be important to you.

Under the terms of our restated certificate of incorporation, our board of directors is authorized to issue up to 5,000,000 shares of preferred stock, par value \$0.0001 per share. Our board of directors may issue shares of preferred stock in one or more series without stockholder approval, and has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock. We may amend from time to time our restated certificate of incorporation to increase the number of authorized shares of preferred stock. Any such amendment would require the approval of the holders of a majority of the voting power of the shares entitled to vote thereon. As of the date of this prospectus, we have 5,000,000 shares of preferred shares authorized, but no shares of preferred stock outstanding.

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It is not possible to state the actual effect of the issuance of any shares of preferred stock upon the rights of the holders of common stock until the board of directors determines the specific rights of the holders of preferred stock. However, effects of the issuance of preferred stock include restricting dividends on common stock, diluting the voting power of common stock, impairing the liquidation rights of common stock, and making it more difficult for a third party to acquire us, which could have the effect of discouraging a third party from acquiring, or deterring a third party from paying a premium to acquire, a majority of our outstanding voting stock.

The particular terms of any series of preferred stock being offered by us will be described in the prospectus supplement relating to that series of preferred stock. Those terms may include:

- the title and liquidation preference per share of the preferred stock and the number of shares offered;
- the purchase price of the preferred stock;
- the dividend rate (or method of calculation);
- the dates on which dividends will be paid and the date from which dividends will begin to accumulate;
- any redemption or sinking fund provisions of the preferred stock;
- any listing of the preferred stock on any securities exchange or market;
- any conversion provisions of the preferred stock;
- the voting rights, if any, of the preferred stock; and
- any additional dividend, liquidation, redemption, sinking fund and other rights, preferences, privileges, limitations and restrictions of the preferred stock.

The preferred stock will, when issued, be fully paid and non-assessable.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase shares of our common stock and/or preferred stock in one or more series together with other securities or separately, as described in each applicable prospectus supplement.

The prospectus supplement relating to any warrants we offer will include specific terms relating to the offering. These terms will include some or all of the following:

- the title of the warrants;
- the aggregate number of warrants offered;
- the designation, number and terms of the shares of common stock purchasable upon exercise of the warrants and procedures by which those numbers may be adjusted;
- the exercise price of the warrants;
- the dates or periods during which the warrants are exercisable;
- the designation and terms of any securities with which the warrants are issued;
- if the warrants are issued as a unit with another security, the date on and after which the warrants and the other security will be separately transferable;
- if the exercise price is not payable in U.S. dollars, the foreign currency, currency unit or composite currency in which the exercise price is denominated;
- any minimum or maximum amount of warrants that may be exercised at any one time;
- any terms relating to the modification of the warrants;
- any terms, procedures and limitations relating to the transferability, exchange or exercise of the warrants; and
- any other specific terms of the warrants.

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities which may be senior, subordinated or junior subordinated and may be convertible. Unless otherwise specified in the applicable prospectus supplement, our debt securities will be issued in one or more series under an indenture to be entered into between us and a trustee. We will issue the debt securities offered by this prospectus and any accompanying prospectus supplement under an indenture to be entered into between us and the trustee identified in the applicable prospectus supplement. The terms of the debt securities will include those stated in the indenture and those made part of the indenture by reference to the Trust Indenture Act of 1939, as in effect on the date of the indenture. We have filed a copy of the form of indenture as an exhibit to the registration statement in which this prospectus is included. The indenture will be subject to and governed by the terms of the Trust Indenture Act of 1939.

The following description briefly sets forth certain general terms and provisions of the debt securities that we may offer. The particular terms of the debt securities offered by any prospectus supplement and the extent, if any, to which these general provisions may apply to the debt securities, will be described in the related prospectus supplement. Accordingly, for a description of the terms of a particular issue of debt securities, reference must be made to both the related prospectus supplement and to the following description.

Debt Securities

The aggregate principal amount of debt securities that may be issued under the indenture is unlimited. The debt securities may be issued in one or more series as may be authorized from time to time pursuant to a supplemental indenture entered into between us and the trustee or an order delivered by us to the trustee. For each series of debt securities we offer, a prospectus supplement accompanying this prospectus will describe the following terms and conditions of the series of debt securities that we are offering, to the extent applicable:

- title and aggregate principal amount;
- whether the debt securities will be senior, subordinated or junior subordinated;
- applicable subordination provisions, if any;
- provisions regarding whether the debt securities will be convertible or exchangeable into other securities or property of the Company or any other person;
- percentage or percentages of principal amount at which the debt securities will be issued;
- maturity date(s);
- interest rate(s) or the method for determining the interest rate(s);
- whether interest on the debt securities will be payable in cash or additional debt securities of the same series;
- dates on which interest will accrue or the method for determining dates on which interest will accrue and dates on which interest will be payable;
- whether the amount of payment of principal of, premium, if any, or interest on the debt securities may be determined with reference to an index, formula or other method;
- redemption, repurchase or early repayment provisions, including our obligation or right to redeem, purchase or repay debt securities under a sinking fund, amortization or analogous provision;
- if other than the debt securities' principal amount, the portion of the principal amount of the debt securities that will be payable upon declaration of acceleration of the maturity;
- authorized denominations;
- form;
- amount of discount or premium, if any, with which the debt securities will be issued, including whether the debt securities will be issued as "original issue discount" securities;
- the place or places where the principal of, premium, if any, and interest on the debt securities will be payable;
- where the debt securities may be presented for registration of transfer, exchange or conversion;
- the place or places where notices and demands to or upon the Company in respect of the debt securities may be made;
- whether the debt securities will be issued in whole or in part in the form of one or more global securities;
- if the debt securities will be issued in whole or in part in the form of a book-entry security, the depository or its nominee with respect to the debt securities and the circumstances under which

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the book-entry security may be registered for transfer or exchange or authenticated and delivered in the name of a person other than the depository or its nominee;

- whether a temporary security is to be issued with respect to such series and whether any interest payable prior to the issuance of definitive securities of the series will be credited to the account of the persons entitled thereto;
- the terms upon which beneficial interests in a temporary global security may be exchanged in whole or in part for beneficial interests in a definitive global security or for individual definitive securities;
- the guarantors, if any, of the debt securities, and the extent of the guarantees and any additions or changes to permit or facilitate guarantees of such debt securities;
- any covenants applicable to the particular debt securities being issued;
- any defaults and events of default applicable to the debt securities, including the remedies available in connection therewith;
- currency, currencies or currency units in which the purchase price for, the principal of and any premium and any interest on, such debt securities will be payable;
- time period within which, the manner in which and the terms and conditions upon which the Company or the purchaser of the debt securities can select the payment currency;
- securities exchange(s) on which the debt securities will be listed, if any;
- whether any underwriter(s) will act as market maker(s) for the debt securities;
- extent to which a secondary market for the debt securities is expected to develop;
- provisions relating to defeasance;
- provisions relating to satisfaction and discharge of the indenture;
- any restrictions or conditions on the transferability of the debt securities;
- provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- any addition or change in the provisions related to compensation and reimbursement of the trustee;
- provisions, if any, granting special rights to holders upon the occurrence of specified events;
- whether the debt securities will be secured or unsecured, and, if secured, the terms upon which the debt securities will be secured and any other additions or changes relating to such security; and
- any other terms of the debt securities that are not inconsistent with the provisions of the Trust Indenture Act (but may modify, amend, supplement or delete any of the terms of the indenture with respect to such series of debt securities).

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General

One or more series of debt securities may be sold as "original issue discount" securities. These debt securities would be sold at a substantial discount below their stated principal amount, bearing no interest or interest at a rate which at the time of issuance is below market rates. One or more series of debt securities may be variable rate debt securities that may be exchanged for fixed rate debt securities.

United States federal income tax consequences and special considerations, if any, applicable to any such series will be described in the applicable prospectus supplement.

Debt securities may be issued where the amount of principal and/or interest payable is determined by reference to one or more currency exchange rates, commodity prices, equity indices or other factors. Holders of such debt securities may receive a principal amount or a payment of interest that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending upon the value of the applicable currencies, commodities, equity indices or other factors. Information as to the methods for determining the amount of principal or interest, if any, payable on any date, the currencies, commodities, equity indices or other factors to which the amount payable on such date is linked and certain additional United States federal income tax considerations will be set forth in the applicable prospectus supplement.

The term "debt securities" includes debt securities denominated in U.S. dollars or, if specified in the applicable prospectus supplement, in any other freely transferable currency or units based on or relating to foreign currencies.

We expect most debt securities to be issued in fully registered form without coupons and in denominations of \$2,000 and any integral multiples thereof. Subject to the limitations provided in the indenture and in the prospectus supplement, debt securities that are issued in registered form may be transferred or exchanged at the principal corporate trust office of the trustee, without the payment of any service charge, other than any tax or other governmental charge payable in connection therewith.

Global Securities

The debt securities of a series may be issued in whole or in part in the form of one or more global securities that will be deposited with, or on behalf of, a depositary identified in the prospectus supplement. Global securities will be issued in registered form and in either temporary or definitive form. Unless and until it is exchanged in whole or in part for the individual debt securities, a global security may not be transferred except as a whole by the depositary for such global security to a nominee of such depositary or by a nominee of such depositary to such depositary or another nominee of such depositary or by such depositary or any such nominee to a successor of such depositary or a nominee of such successor. The specific terms of the depositary arrangement with respect to any debt securities of a series and the rights of and limitations upon owners of beneficial interests in a global security will be described in the applicable prospectus supplement.

Governing Law

The indenture and the debt securities shall be construed in accordance with and governed by the laws of the State of New York.

DESCRIPTION OF UNITS

We may issue, in one more series, units comprised of shares of our common stock or preferred stock, warrants to purchase common stock or preferred stock, debt securities or any combination of those securities. 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 may evidence units by unit certificates that we issue under a separate agreement. We may issue the units under a unit agreement between us and one or more unit agents. If we elect to enter into a unit agreement with a unit agent, the unit agent will act solely as our agent in connection with the units and will not assume any obligation or relationship of agency or trust for or with any registered holders of units or beneficial owners of units. We will indicate the name and address and other information regarding the unit agent in the applicable prospectus supplement relating to a particular series of units if we elect to use a unit agent.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

- 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;
- any provisions of the governing unit agreement that differ from those described herein; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The other provisions regarding our common stock, preferred stock, warrants and debt securities as described in this section will apply to each unit to the extent such unit consists of shares of our common stock, preferred stock, warrants and/or debt securities.

PLAN OF DISTRIBUTION

We may sell the securities covered in this prospectus from time to time in one or more of the following ways:

- through underwriters or dealers;
- in short or long transactions;
- directly to a limited number of purchasers or to a single purchaser;
- through agents; or
- through a combination of any of these methods of sale.

Each time that we use this prospectus to sell securities, we will also provide a prospectus supplement that contains the specific terms of the offering. The prospectus supplement will set forth the terms of the offering of the securities, including:

- the name or names of any underwriters, dealers or agents and the amounts of any securities underwritten or purchased by each of them; and
- the purchase price of the securities being offered and the proceeds to us and any discounts, commissions or concessions allowed or reallocated or paid to dealers.

The purchase price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

If underwriters are used in the sale of any securities, the securities will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. The securities may be either offered to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters. Generally, the underwriters' obligations to purchase the securities will be subject to certain conditions precedent. The underwriters will be obligated to purchase all of the securities if they purchase any of the securities.

We may sell the securities through agents from time to time. The prospectus supplement will name any agent involved in the offer or sale of the securities and any commissions we pay to them. Generally, any agent will be acting on a best efforts basis for the period of its appointment.

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

Agents and underwriters may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act of 1933, as amended, or to contribution with respect to payments which the agents or underwriters may be required to make in respect thereof. Agents and underwriters may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

We may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of securities, and may use securities received from us in

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settlement of those derivatives to close out any related open borrowings of securities. The third party in such sale transactions will be an underwriter and will be identified in the applicable prospectus supplement (or a post-effective amendment). We may also use underwriters or such other third parties with whom we have a material relationship. We will describe the nature of any such relationship in the applicable prospectus supplement.

In compliance with the guidelines of the Financial Industry Regulatory Authority, Inc., or FINRA, the maximum compensation to be received by a FINRA member or independent broker-dealer may not exceed 8% of the offering proceeds. It is anticipated that the maximum compensation to be received in any particular offering of securities will be less than this amount.

At-the-Market Offerings

Upon written instruction from us, a sales agent party to a distribution agency agreement with us will use its commercially reasonable efforts to sell on our behalf, as our agent, the shares of common stock offered as agreed upon by us and the sales agent. We will designate the maximum amount of shares of common stock to be sold through the sales agent, on a daily basis or otherwise as we and the sales agent agree. Subject to the terms and conditions of the applicable distribution agency agreement, the sales agent will use its commercially reasonable efforts to sell, as our sales agent and on our behalf, all of the designated shares of common stock. We may instruct the sales agent not to sell shares of common stock if the sales cannot be effected at or above the price designated by us in any such instruction. We may suspend the offering of shares of common stock under any distribution agency agreement by notifying the sales agent. Likewise, the sales agent may suspend the offering of shares of common stock under the applicable distribution agency agreement by notifying us of such suspension.

We also may sell shares to the sales agent as principal for its own account at a price agreed upon at the time of sale. If we sell shares to the sales agent as principal, we will enter into a separate agreement setting forth the terms of such transaction.

The offering of common stock pursuant to a distribution agency agreement will terminate upon the earlier of (1) the sale of all shares of common stock subject to the distribution agency agreement or (2) the termination of the distribution agency agreement by us or by the sales agent.

Sales agents under our distribution agency agreements may make sales in privately negotiated transactions and/or any other method permitted by law, including sales deemed to be an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act, sales made directly on the Nasdaq Capital Market, the existing trading market for our common stock, or sales made to or through a market maker other than on an exchange. The name of any such underwriter or agent involved in the offer and sale of our common stock, the amounts underwritten, and the nature of its obligations to take our common stock will be described in the applicable prospectus supplement.

LEGAL MATTERS

The legality and validity of the securities offered from time to time under this prospectus will be passed upon by Alston & Bird LLP, New York, New York.

EXPERTS

The financial statements of Stemline Therapeutics, Inc. appearing in Stemline Therapeutics, Inc's Annual Report (Form 10-K) for the year ended December 31, 2016 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

Up to \$50,000,000



Common stock

Prospectus supplement

J.P. Morgan

Cantor

Ladenburg Thalmann

March 16, 2018
