

Ampio Pharmaceuticals, Inc.
Form 424B5
April 15, 2019
Table of Contents

Filed Pursuant to Rule 424(b)(5)

Registration No. 333 217094

PROSPECTUS SUPPLEMENT

(to Prospectus dated April 20, 2017)

Up to \$24,650,000

Common Stock

We have entered into an Equity Distribution Agreement with Canaccord Genuity LLC (Canaccord) relating to shares of our common stock, \$0.0001 par value per share, offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the Equity Distribution Agreement, we may offer and sell shares of our common stock from time to time up to an aggregate offering price of \$24,650,000 through Canaccord, acting as sales agent.

We are, at this time, subject to General Instruction I.B.6 of Form S-3, which limits the amounts that we may sell under the registration statement which includes this prospectus supplement. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities registered on the registration statement of which this prospectus supplement is a part in a public primary offering with a value exceeding more than one-third of our public float in any 12 month period if our public float, measured in accordance with the instruction, remains below \$75,000,000. The aggregate market value of our common stock held by non-affiliates pursuant to General Instruction I.B.6. of Form S-3 is \$73,969,488, which was calculated based on 108,778,659 shares of our outstanding common stock held by non-affiliates on March 4, 2019 at a price of \$0.68 per share, the closing price of our common stock on March 4, 2019. As of the date hereof, we have not sold any securities pursuant to General Instruction I.B.6 of Form S-3 during the 12 calendar months prior to and including the date of this prospectus supplement. As a result of the limitations of General Instruction I.B.6, and in accordance with the terms of the Equity Distribution Agreement, we are registering the offer and sale of shares of our common stock having an aggregate offering price of up to \$24,650,000 from time to time through Canaccord.

Upon our delivery of a placement notice and subject to the terms and conditions of the Equity Distribution Agreement, Canaccord may sell the 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 (the Securities Act), including sales made directly on the New York Stock Exchange American market, on any other existing trading market for the common stock or to or through a market maker other than on an exchange. In addition, with our prior written approval, Canaccord may also sell the common stock by any other method permitted by law, including in privately negotiated transactions. Canaccord 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 New York Stock Exchange American market. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

We will pay Canaccord a commission, or allow a discount, for its services in acting as agent in the sale of common stock equal to 3.0% of the gross sales price per share of all shares sold through it as agent under the Equity Distribution Agreement. See “Plan of Distribution” for information relating to certain expenses of Canaccord to be

reimbursed by us.

In connection with the sale of common stock on our behalf, Canaccord may be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation to Canaccord will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Canaccord with respect to certain liabilities, including liabilities under the Securities Act.

Table of Contents

Our common stock is listed on the New York Stock Exchange American market under the symbol “AMPE.” The last sale price of our common stock on April 11, 2019, as reported by the New York Stock Exchange American market, was \$0.5033 per share.

We are a smaller reporting company under Rule 405 of the Securities Act and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus supplement, the documents incorporated by reference herein and future filings.

As of April 11, 2019, the aggregate market value of our outstanding common stock held by non-affiliates was approximately \$54,748,299 based on 111,127,878 shares of outstanding common stock, of which 2,349,219 shares are held by affiliates, at a price of \$0.5033 per share, which was the last reported trading price of our common stock on the New York Stock Exchange American market on April 11, 2019.

Investing in our common stock involves a high degree of risk. See “Risk Factors” beginning on page S 8 of this prospectus supplement and page 6 of the accompanying base prospectus, as well as the information under the caption “Risk Factors” in our Annual Report on Form 10 K for the year ended December 31, 2018 and in the other documents incorporated by reference into this prospectus supplement and the accompanying prospectus for a discussion of the factors you should carefully consider before investing in our common stock.

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 base prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Canaccord Genuity

Prospectus Supplement dated April 12, 2019.

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

<u>ABOUT THIS PROSPECTUS SUPPLEMENT</u>	S-2
<u>FORWARD-LOOKING STATEMENTS</u>	S-3
<u>PROSPECTUS SUMMARY</u>	S-4
<u>THE OFFERING</u>	S-7
<u>RISK FACTORS</u>	S-8
<u>USE OF PROCEEDS</u>	S-11
<u>DIVIDEND POLICY</u>	S-12
<u>DILUTION</u>	S-13
<u>CERTAIN U.S. FEDERAL INCOME TAX CONSIDERATIONS</u>	S-14
<u>PLAN OF DISTRIBUTION</u>	S-19
<u>DESCRIPTION OF CAPITAL STOCK</u>	S-21
<u>LEGAL MATTERS</u>	S-22
<u>EXPERTS</u>	S-22
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	S-23
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	S-23
<u>Prospectus</u>	
<u>ABOUT THIS PROSPECTUS</u>	1
<u>SUMMARY</u>	1
<u>RISK FACTORS</u>	5
<u>FORWARD-LOOKING STATEMENTS</u>	5
<u>RATIO OF EARNINGS TO COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS</u>	7
<u>USE OF PROCEEDS</u>	8
<u>SELLING STOCK HOLDERS</u>	9

<u>PLAN OF DISTRIBUTION</u>	11
<u>DESCRIPTION OF CAPITAL STOCK</u>	14
<u>DESCRIPTION OF DEBT SECURITIES</u>	19
<u>DESCRIPTION OF WARRANTS</u>	26
<u>DESCRIPTION OF UNITS</u>	27
<u>LEGAL MATTERS</u>	28
<u>EXPERTS</u>	28
<u>WHERE YOU CAN FIND ADDITIONAL INFORMATION</u>	28
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	28

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus relate to the offering of shares of our common stock. Before buying any shares of our common stock offered hereby, we urge you to carefully read this prospectus supplement and the accompanying prospectus, together with the information incorporated herein and therein by reference as described under the headings “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.” These documents contain important information that you should consider when making your investment decision.

On March 31, 2017, we filed with the Securities and Exchange Commission (the SEC) a registration statement on Form S-3 (File No. 333-217094) utilizing a shelf registration process relating to the securities described in this prospectus supplement, which registration statement became effective on April 20, 2017. Under this shelf registration process, we may, from time to time, sell common stock and other securities, including this offering.

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 into the prospectus and this prospectus supplement. The second part, the accompanying prospectus dated April 20, 2017, including the documents incorporated by reference therein, gives more general information, some of which does not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined.

If the description of the offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information contained in this prospectus supplement. However, 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 — the statement in the document having the later date modifies or supersedes the earlier statement. In particular, with respect to any information contained in this prospectus supplement, on the one hand, and information in the accompanying prospectus or documents incorporated by reference, on the other hand, the information in this prospectus supplement shall control.

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 prospectus supplement or 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.

The industry and market data and other statistical information contained herein or in the documents we incorporate by reference are based on management’s own estimates, independent publications, government publications, reports by market research firms or other published independent sources and, in each case, are believed by management to be reasonable estimates. Although we believe these sources are reliable, we have not independently verified the information.

All references in this prospectus supplement and the accompanying base prospectus to “Ampio,” “Ampio Pharmaceuticals Inc.,” the “Company,” “we,” “us,” “our” or similar references refer to Ampio Pharmaceuticals, Inc. and its subsidiaries on a consolidated basis, except where the context otherwise requires or as otherwise indicated.

AMPIO (and design), our logo design and AMPION are our registered trademarks. This prospectus also contains trademarks, registered marks and trade names of other companies. Any other trademarks, registered marks and trade

names appearing in this prospectus are the property of their respective holders.

S-2

Table of Contents

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying base prospectus and the documents incorporated by reference in these documents contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. All statements other than statements of historical facts contained in this prospectus supplement, including statements regarding our anticipated future clinical and regulatory events, future financial position, business strategy and plans and objectives of management for future operations, are forward-looking statements. Forward looking statements are generally written in the future tense and/or are preceded by words such as “may,” “will,” “should,” “forecast,” “could,” “expect,” “suggest,” “believe,” “estimate,” “continue,” “anticipate,” “intend,” “plan” or similar words, or the negatives of such terms or other variations on such terms or comparable terminology. Such forward-looking statements include, without limitation, statements regarding the anticipated start dates, durations and completion dates, as well as the potential future results, of our future clinical trials, the anticipated designs of our future clinical trials, anticipated future regulatory submissions and events, regulatory responses or other actions in relation to our submissions, applications and proposals, the potential future commercialization of our product candidate, Ampion, our anticipated future cash position and future events under our current and potential future collaborations. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including without limitation the risks described in the “Risk Factors” section in this prospectus supplement. These risks are not exhaustive. Other sections of this prospectus supplement include additional factors that could adversely impact our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. We assume no obligation to update or supplement forward-looking statements.

We obtained statistical data, market and product data, and forecasts used throughout this prospectus supplement from market research, publicly available information and industry publications. While we believe that the statistical data, industry data and forecasts and market research are reliable, we have not independently verified the data, and we do not make any representation as to the accuracy of the information.

All written and verbal forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. We caution investors not to rely too heavily on the forward-looking statements we make or that are made on our behalf. We undertake no obligation, and specifically decline any obligation, to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

The following summary is qualified in its entirety by, and should be read together with, the more detailed information and financial statements and related notes thereto appearing elsewhere or incorporated by reference in this prospectus supplement and the accompanying base prospectus. Before you decide to invest in our common stock, you should read the entire prospectus supplement and the accompanying base prospectus carefully, including the risk factors and the financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying base prospectus.

About Ampio Pharmaceuticals, Inc.

Overview

Our focus is on developing Ampion, which is a compound that decreases inflammation by inhibiting specific pro-inflammatory compounds.

Ampion has advanced through late-stage clinical trials in the United States. The U.S. Food and Drug Administration, or FDA, provided guidance that we should complete a trial of Kellgren Lawrence Grade 4, or KL 4, osteoarthritis patients with concurrent controls that would be carried out under a Special Protocol Assessment, or SPA, or otherwise with FDA feedback. An SPA is a process in which sponsors may ask to meet with FDA to reach agreement on the design and size of certain clinical trials to determine if they adequately address scientific and regulatory requirements for a study that could support marketing approval. An SPA agreement would indicate concurrence by FDA with the adequacy and acceptability of specific critical elements of overall protocol design for the trial of KL 4 osteoarthritis patients with concurrent controls, which study is intended to support our future Biologic Licensing Application, or BLA. The elements of the study agreed upon in the SPA agreement are critical to ensuring that the trial conducted under the protocol can be considered an adequate and well-controlled study that can support marketing licensure of Ampion. However, an SPA agreement will not indicate FDA concurrence on every protocol detail, and FDA may still require us to conduct additional clinical trials in the future to support a BLA for Ampion.

Ampion for Osteoarthritis and Other Inflammatory Conditions

Ampion is the < 5 kDa ultrafiltrate of 5% Human Serum Albumin, or HSA, which is an FDA approved biologic product. Ampion is a non-steroidal, low molecular weight, anti-inflammatory biologic that has the potential to be used in a wide variety of acute and chronic inflammatory conditions, as well as immune-mediated diseases. Ampion and its known components have demonstrated anti-inflammatory activity, which supports the mechanism of action.

We are currently developing Ampion as an intra-articular injection to treat the signs and symptoms of severe osteoarthritis of the knee, or OAK, which is a growing epidemic in the United States. OAK is a progressive disease characterized by gradual degradation and loss of cartilage due to inflammation of the soft tissue and bony structures of the knee joint. Progression of the most severe form of OAK leaves patients with little to no treatment options other than a total knee arthroplasty. The FDA has stated that severe OAK is an ‘unmet medical need’ with no licensed therapies for this indication. While we believe that Ampion could treat this ‘unmet medical need’, our ability to market this product is subject to FDA approval.

Market Opportunity

Osteoarthritis, or OA, is the most common form of arthritis, affecting over 30 million people in the United States. It is a progressive disorder of the joints involving degradation of the intra-articular cartilage, joint lining, ligaments and bone. Certain risk factors in conjunction with natural wear and tear lead to the breakdown of cartilage. Osteoarthritis

is caused by inflammation of the soft tissue and bony structures of the joint, which worsens over time and leads to progressive thinning of articular cartilage. Other progressive effects include narrowing of the joint space, synovial membrane thickening, osteophyte formation and increased density of the subchondral bone. The global market size for treatments that currently address moderate to moderately severe OA was valued at approximately \$3.0 billion in 2016 and is expected to grow with a compound annual growth rate of 9.04% through 2025. The global demand for osteoarthritis of

S-4

Table of Contents

the knee treatment is expected to be fueled by aging demographics and increased awareness of treatment options. Despite the size and growth of the osteoarthritis of the knee market, only a few treatment options currently exist, especially in the severely diseased patient population.

Ampion Development

Since our inception, we have conducted multiple clinical trials and have advanced through late-stage clinical trials in the United States, initially under the guidance of the FDA's Office of Blood Research and Review, or OBRR, and most recently under the guidance of the FDA's Office of Tissues and Advanced Therapies, or OTAT.

Study AP 003 A was a U.S. multicenter, randomized, double-blind trial of 329 patients who were randomized 1:1 to receive Ampion or saline control via intra-articular injection. The study showed a statistically significant reduction in pain compared to the control, with an average of greater than 40% reduction in pain from baseline at 12 weeks. Patients who received Ampion also showed a significant improvement in function and quality of life (quality of life was assessed using the Patient Global Assessment, or PGA) compared to patients who received the saline control at 12 weeks. Furthermore, the trial included severely diseased patients (defined as KL 4). From this patient population, those patients who received Ampion had a significantly greater reduction in pain than those who received the saline control. Ampion was well tolerated with minimal adverse events reported across the Ampion and saline groups in the study. There were no drug-related serious adverse events.

The trial design of AP 003 C was initiated while we were under the guidance of OBRR and modified when guidance was transferred to OTAT in 2017. The study evaluated the responder rate of Ampion-treated patients as defined by the Osteoarthritis Research Society International ("OARSI") Standing Committee for Clinical Trials Response Criteria Initiative (OMERACT), which included pain, function and PGA in support of a label for the treatment of the signs and symptoms of severe OAK at 12 weeks.

Both OBRR and OTAT have confirmed that our successful pivotal phase III clinical trial, AP 003 A, was adequate and well-controlled and provided evidence of the effectiveness of Ampion and can contribute to the substantial evidence of effectiveness necessary for the approval of a Biologics License Application, or BLA. However, OTAT does not consider the AP 003 C trial to be an adequate and well-controlled pivotal trial and provided guidance that we should complete an additional trial of KL 4 osteoarthritis patients with concurrent controls that would be carried out under an SPA to obtain FDA concurrence on the trial design. An SPA would provide a written agreement between us and the FDA indicating concurrence by the FDA on the adequacy and acceptability of specific critical elements of overall protocol design for a study intended to support a future marketing application. The existence of an SPA agreement does not indicate FDA concurrence on every protocol detail or guarantee that the trial results will be adequate to support marketing approval of Ampion. Those issues are addressed during the review of a submitted application and are determined based on the adequacy of the overall submission. We do not plan to begin our KL 4 clinical trial until we are awarded an SPA agreement from the FDA. Should the FDA award the SPA agreement, we plan to commence enrollment of patients. Even if an SPA agreement is awarded, the FDA could rescind the agreement if it becomes aware of a substantial scientific issue and the FDA could change its position regarding critical design elements previously agreed to. Even if the proposed KL 4 trial is completed, the FDA may require additional clinical trials in the future. We cannot ensure that the data derived from the proposed KL 4 trial or any subsequent trial or trials will be sufficient to support marketing approval for Ampion.

Ampion Manufacturing Facility

In December 2013, we entered into a ten-year lease of a multi-purpose facility containing approximately 19,000 square feet. This facility includes a clean room to manufacture Ampion, research laboratories and our corporate offices. Ampion manufactured at our facilities is used in our clinical trials.

We moved into this manufacturing facility in the summer of 2014 and it was placed into service during the first quarter of 2016. Since then, we have implemented a quality system, validated the facility for human-use products and produced Ampion.

S-5

Table of Contents

Recent Developments

As of March 31, 2019, we had cash and cash equivalents of approximately \$5.2 million as compared to approximately \$7.6 million as of December 31, 2018.

This preliminary estimate has been prepared by, and is the responsibility of, our management. Our independent registered public accounting firm, Plante & Moran PLLC, has not audited or reviewed, and does not express an opinion with respect to, these estimates. Actual results and financial data as of March 31, 2019 may differ from the above estimate due to the completion of our closing procedures with respect to the three months ended March 31, 2019, final adjustments and other developments that may arise between now and the time the financial results for the first quarter are finalized.

Corporate Information

We are a Delaware corporation. Our principal offices are located at 373 Inverness Parkway, Suite 200, Englewood, Colorado 80112, and our telephone number is (720) 437-6500. Our website address is www.ampiopharma.com. Our website and the information contained on, or that can be accessed through, our website shall not be deemed to be incorporated by reference in, and are not considered part of, this prospectus and our reference to the URL for our website is intended to be an inactive textual reference only. You should not rely on any such information in making your decision whether to purchase our common stock.

S-6

Table of Contents

THE OFFERING

The following summary contains basic information about this offering. The summary is not intended to be complete. You should read the full text and more specific details contained elsewhere in this prospectus supplement and the accompanying base prospectus.

Common stock offered by us	Shares of our common stock having an aggregate offering price of up to \$24,650,000.
Common stock to be outstanding after this offering	Up to 160,104,631 shares, assuming sales at a price of \$0.5033 per share, which was the closing price of our common stock on the New York Stock Exchange American market on April 11, 2019. The actual number of shares issued will vary depending on the sales price under this offering.
Plan of Distribution	“At the market offering” that may be made from time to time through Canaccord, our sales agent. See the section titled “Plan of Distribution.”
Use of proceeds	We intend to use the net proceeds from this offering for working capital and other general corporate purposes. See the section titled “Use of Proceeds.”
Risk Factors	You should read the “Risk Factors” section of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to purchase shares of our common stock.
The New York Stock Exchange American symbol	AMPE

The number of shares of common stock that will be outstanding immediately after this offering as shown above is based on 111,127,878 shares of common stock outstanding as of April 11, 2019, which includes:

- 110,941,516 shares of our common stock outstanding at December 31, 2018;
- 50,000 shares of our common stock issued pursuant to the exercise of outstanding warrants following December 31, 2018;
- 136,362 shares of our common stock issued under our 2010 Stock Option and Incentive Plan (the 2010 Plan) following December 31, 2018;

and excludes:

- 22,233,191 shares of our common stock issuable upon the exercise of outstanding warrants;
- 5,426,165 shares of our common stock issuable upon the exercise of outstanding options under the 2010 Plan as of December 31, 2018, with a weighted average exercise price of \$1.99 per share; and
- 4,229,783 shares of our common stock reserved for issuance under the 2010 Plan.

Unless otherwise indicated, all information in this prospectus assumes no conversion of preferred stock, exercise of the outstanding options or warrants or settlement of outstanding restricted stock units, described above.

Table of Contents

RISK FACTORS

An investment in our common stock involves a high degree of risk. You should carefully consider the risks described under “Risk Factors” in our most recent Annual Report on Form 10-K and all of the other information contained in this prospectus supplement and the accompanying base prospectus, and incorporated by reference into this prospectus supplement and the accompanying base prospectus, including our financial statements and related notes, before investing in our common stock. If any of the possible adverse events described below or in those sections actually occur, our business, business prospects, cash flow, results of operations or financial condition could be harmed, the trading price of our common stock could decline, and you might lose all or part of your investment in our common stock. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our operations and results.

Risks Related to This Offering and Our Common Stock

An active trading market for our common stock may not develop or be sustained and investors may not be able to resell their shares at or above the price at which they purchased them.

An active trading market for our shares may never develop or be sustained. In the absence of an active trading market for our common stock, investors may not be able to sell their common stock at or above the price they paid or at the time that they would like to sell. In addition, an inactive market may impair our ability to raise capital by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration, which, in turn, could harm our business.

The trading price of the shares of our common stock has been and is likely to continue to be highly volatile, and purchasers of our common stock could incur substantial losses.

Our stock price has been and will likely continue to be volatile for the foreseeable future. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the price they paid.

In addition, in the past, stockholders have initiated class action lawsuits against biotechnology and pharmaceutical companies including us following periods of volatility in the market prices of these companies’ and our stock. Such litigation, including the litigation that is currently instituted against us and certain of our officers and directors and any litigation that may be instituted against us, our officers and/or our directors in the future, could cause us to incur substantial costs and divert management’s attention and resources, which could have a material adverse effect on our business, financial condition and results of operations.

Our quarterly operating results may fluctuate significantly.

We expect that our operating results may be subject to substantial quarterly fluctuations. If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

You will experience immediate and substantial dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of \$24,650,000 of shares of our common stock are sold

at the assumed offering price of \$0.5033 per share (the last reported sale price of our common stock on the New York Stock Exchange American market on April 11, 2019), and after deducting commissions and estimated aggregate offering expenses payable by us, you will experience immediate dilution of \$0.32 per share, representing the difference between our as adjusted net tangible book value per share as of December 31, 2018 after giving effect to this offering and the assumed offering price. In addition, we are not restricted from issuing additional securities in the future, including shares

S-8

Table of Contents

of common stock, securities that are convertible into or exchangeable for, or that represent the right to receive, common stock or substantially similar securities. The issuance of these securities may cause further dilution to our stockholders. The exercise of outstanding stock options and the vesting of outstanding restricted stock units may also result in further dilution of your investment. See the section entitled “Dilution” on page S 14 below for a more detailed illustration of the dilution you may incur if you participate in this offering.

We may allocate our cash and cash equivalents, including the proceeds from this offering, in ways that you and other stockholders may not approve.

Our management has broad discretion in the application of our cash, cash equivalents and marketable securities, including the proceeds from this offering. Because of the number and variability of factors that will determine our use of our cash and cash equivalents, their ultimate use may vary substantially from their currently intended use. Our management might not apply our cash and cash equivalents in ways that ultimately increase the value of your investment. We expect to use our cash and cash equivalents to fund Ampion clinical trials, working capital and other general corporate purposes. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest our cash and cash equivalents in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders. If we do not invest or apply our cash and cash equivalents, including the proceeds from this offering, in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

A substantial number of shares of our common stock could be sold into the public market in the near future, which could depress our stock price.

Sales of substantial amounts of our common stock in the public market could reduce the prevailing market prices for our common stock. Substantially all of our outstanding common stock are eligible for sale as are common stock issuable under vested and exercisable stock options. If our existing stockholders sell a large number of shares of our common stock, or the public market perceives that existing stockholders might sell shares of common stock, the market price of our common stock could decline significantly. These sales might also make it more difficult for us to sell equity securities at a time and price that we deem appropriate.

If securities or industry analysts do not publish research or reports or publish unfavorable research or reports about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. We currently have limited research coverage by securities and industry analysts. If other securities or industry analysts do not commence coverage of our company, the trading price for our stock could be negatively impacted. If one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

We are defendants in securities and shareholder litigations and could be subject to additional litigations.

The company and certain of its officers and directors are currently defendants in pending shareholder derivative actions and/or putative class actions for violations of the federal securities laws.

Specifically, as disclosed in our Form 10 K for the period ended December 31, 2018, on August 31, 2018, a stockholder of the Company brought a putative class action lawsuit in the United States District Court for the Central District of California, Shi v. Ampio Pharmaceuticals, Inc., et al., Case No. 2:18 cv 07476 SJO-RAO, which alleges that

the Company and certain of its current officers violated federal securities laws by misrepresenting and/or omitting information regarding the AP 003 Phase III clinical trials of Ampion and seeks unspecified damages, interest, and attorneys' fees and costs. Additionally, on September 10, 2018, October 5, 2018 and November 14, 2018, three separate purported stockholders of the Company brought derivative actions against the Company in the United States District Court for the Central District of California, Cetrone v. Macaluso, et al., Case No. 2:18 cv 05970 SJO-RAO, the United

S-9

Table of Contents

States District Court for the District of Colorado, Theise v. Macaluso, et al., Case No. 1:18 cv 02558 RBJ and United States District Court for the District of Colorado, Lewis v. Macaluso, et al., Case No. 1:18 cv 02932 SKC, respectively, each alleging primarily that the directors and officers of Ampio breached their fiduciary duties in connection with the alleged misstatements and/or omissions regarding the AP 003 Phase III clinical trial of Ampion. On December 19, 2018, the court consolidated the Theise and Lewis derivative actions, and the consolidated action is captioned In re Ampio Pharmaceuticals, Inc. Stockholder Derivative Litigation, Case No. 1:18 cv 02558 RBJ.

While, we believe that all claims asserted are without merit and intend to defend these lawsuits vigorously, it is possible that additional actions will be filed in the future. Additionally, while we believe our Directors and Officers Liability Insurance (D&O Insurance) will cover the current actions, the current and any future actions could result in substantial cost to the Company through our payment of the \$1 million retention under our D&O Insurance and/or if our insurer denies coverage. The current actions could also result in a diversion of management's attention and resources. The incurrence of substantial cost or diversion of management's attention could each have a material adverse effect on our business, financial condition and results of operations.

S-10

Table of Contents

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of our securities offered hereby. Except as described in any free writing prospectus that we may authorize to be provided to you, we currently anticipate using the net proceeds from the sale of our securities offered hereby primarily for working capital, including the conduct of a clinical trial, and other general corporate purposes. Further, from time to time we may evaluate acquisition opportunities and engage in related discussions with other companies. We do not currently have any intentions with respect to the acquisition of or investment in complementary businesses, products or technologies. As of the date hereof, the Company does not have any debt to service.

The amounts and timing of our use of the net proceeds from this offering, if any, will depend on a number of factors, such as the timing and progress of our research and development efforts, the timing and progress of any partnering and collaboration efforts and technological advances. 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 this offering. Accordingly, our management will have broad discretion in the timing and application of these proceeds. Pending use of the proceeds as described above, we intend to invest the proceeds in a variety of capital preservation investments, including short term, interest bearing, investment grade instruments and U.S. government securities.

S-11

Table of Contents

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination to declare cash dividends will be made at the discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

S-12

Table of Contents

DILUTION

If you invest in this offering, your ownership interest will be immediately diluted to the extent of the difference between the public offering price per share and the as adjusted net tangible book value per share after giving effect to this offering. We calculate net tangible book value per share by dividing the net tangible book value, which is the total tangible assets less total liabilities, by the number of outstanding shares of our common stock. Dilution represents the difference between the portion of the amount per share paid by purchasers of shares in this offering and the as adjusted net tangible book value per share of our common stock immediately after giving effect to this offering. Our net tangible book value as of December 31, 2018 was approximately \$5.2 million, or \$0.05 per share.

After giving effect to the assumed sale of 48,976,753 shares of our common stock during the term of the equity distribution agreement with Canaccord in the aggregate amount of \$24,650,000 at an assumed offering price of \$0.5033 per share, the last reported sale price of our common stock on the New York Stock Exchange American market on April 11, 2019, and after deducting commissions and estimated aggregate offering expenses payable by us, our net tangible book value as of December 31, 2018 would have been approximately \$29.0 million, or approximately \$0.18 per share of common stock. This represents an immediate increase in the net tangible book value of approximately \$0.13 per share to our existing stockholders and an immediate dilution in net tangible book value of approximately \$0.32 per share to new investors.

The following table illustrates this per share dilution based on shares outstanding as of December 31, 2018:

Assumed public offering price per share		\$ 0.5033
Historical net tangible book value per share as of December 31, 2018	\$ 0.05	
Increase in net tangible book value per share after this offering	\$ 0.13	
As-Adjusted Net tangible book value per share as of December 31, 2018 after this offering		\$ 0.18
Dilution per share to investors participating in this offering		\$ 0.32

The above discussion and tables excludes:

- 50,000 shares of our common stock issued pursuant to the exercise of outstanding warrants following December 31, 2018;
- 136,362 shares of our common stock issued under the 2010 Plan following December 31, 2018;
- 22,233,191 shares of our common stock issuable upon the exercise of outstanding warrants;
- 5,426,165 shares of our common stock issuable upon the exercise of outstanding options under the 2010 Plan as of December 31, 2018, with a weighted average exercise price of \$1.99 per share; and
- 4,366,145 shares of our common stock reserved for issuance under the 2010 Plan as of December 31, 2018.

After giving effect to the sale of our common stock during the term of the equity distribution agreement with Canaccord in the aggregate amount of \$24,650,000 at an assumed offering price of \$0.5033 per share, the last reported sale price of our common stock on the New York Stock Exchange American market on April 11, 2019, and after deducting commissions and estimated aggregate offering expenses payable by us, on an as-adjusted pro forma basis assuming 159,918,269 outstanding common shares, consisting of shares outstanding as of December 31, 2018 our net tangible book value as of December 31, 2018 would have been approximately \$29.0 million, or approximately \$0.18 per share of common stock. On an as-adjusted pro forma basis, this represents an immediate increase in the net tangible book value of approximately \$0.13 per share to our existing stockholders and an immediate dilution in net tangible book value of approximately \$0.32 per share to new investors.

To the extent that any of these options or warrants are exercised, new options are issued under our 2010 Plan and subsequently exercised or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering.

S-13

Table of Contents

CERTAIN U.S. FEDERAL INCOME TAX CONSIDERATIONS

This section summarizes certain U.S. federal income tax considerations relating to the purchase, ownership and disposition of common stock issued pursuant to this offering. This summary does not provide a complete analysis of all potential tax considerations. The information provided below is based upon provisions of the Internal Revenue Code of 1986, as amended, or the Code, Treasury regulations promulgated thereunder and administrative rulings and judicial decisions, all as currently in effect. These authorities may change at any time, possibly on a retroactive basis, or the U.S. Internal Revenue Service, or the IRS, might interpret the existing authorities differently. In either case, the tax considerations of purchasing, owning or disposing of common stock could differ from those described below. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership and disposition of common stock.

This discussion is limited to holders that hold the common stock as a “capital asset” within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all of the U.S. federal income tax considerations that might be relevant to a beneficial owner in light of such beneficial owner’s particular circumstances, such as the impact of the Medicare contribution tax on net investment income or alternative minimum tax. In addition, this discussion does not address tax considerations to beneficial owners subject to special treatment under the U.S. federal income tax laws, including:

- a broker, dealer or trader in securities, currencies, commodities or notional principal contracts;
- a bank, financial institution or insurance company;
- a regulated investment company, a real estate investment trust or grantor trust;
- a tax-exempt entity or organization, including an individual retirement account or Roth IRA as defined in Section 408 or 408A of the Code, respectively;
- a person holding the common stock as part of a hedging, integrated or conversion transaction or a straddle, or a person deemed to sell common stock under the constructive sale provisions of the Code;
- a trader in securities that has elected the mark-to-market method of tax accounting for securities;
- an entity that is treated as a partnership or other pass-through entity for U.S. federal income tax purposes;
- a person who is a partner or investor in a partnership or other pass-through entity that holds the common stock;
- a U.S. person whose “functional currency” is not the U.S. dollar;
- a controlled foreign corporation or passive foreign investment company;
- a person who holds or receives common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- a qualified foreign pension fund or an entity that is wholly owned by one or more qualified foreign pension funds;
or
- a U.S. expatriate and former citizens or long-term residents of the United States.

Table of Contents

For purposes of this discussion, a “U.S. holder” is a beneficial owner of a share of common stock that is, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation (or any other entity treated as a corporation for U.S. federal income tax purposes) created or organized in or under the laws of the United States, any state thereof or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if (1) it is subject to the primary supervision of a court within the United States and one or more U.S. persons have the authority to control all substantial decisions of the trust or (2) it has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

For purposes of this discussion, a “non-U.S. holder” is a beneficial owner of a share of common stock that is (i) a foreign corporation for U.S. federal income tax purposes, (ii) a nonresident alien individual or (iii) a foreign estate or trust that in each case is not subject to U.S. federal income tax on a net-income basis on income or gain from a share of common stock.

If an entity treated as a partnership for U.S. federal income tax purposes holds shares of common stock, the tax treatment of a person treated as a partner in such partnership will generally depend upon the status of the partner and the activities of the partnership. This discussion does not address the tax considerations to an entity treated as a partnership for U.S. federal income tax purposes or any investor in such entity. Accordingly, a partnership holding shares of common stock and any partner therein should consult their own tax advisors as to the tax consequences of holding and disposing of common stock.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock arising under the U.S. federal estate or gift tax rules or under the laws of any U.S. state or local or any non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

Certain U.S. Federal Income Tax Considerations for U.S. Holders of Common Stock

Dividends on our Common Stock

We do not expect to declare or pay any distributions on our common stock in the foreseeable future. If we do make any distributions on shares of our common stock, such distributions will be includible in the gross income of a U.S. holder as ordinary dividend income to the extent paid out of current or accumulated earnings and profits, as determined for U.S. federal income tax purposes. Any portion of a distribution in excess of current or accumulated earnings and profits will be treated as a return of the holder’s tax basis in its common stock and then as gain from the sale or exchange of the common stock. Under current law, if certain requirements are met, a preferential U.S. federal income tax rate will apply to any dividends paid to a holder of common stock who is a U.S. individual.

Distributions to U.S. holders that are corporate shareholders, constituting dividends for U.S. federal income tax purposes, may qualify for the dividends received deduction, or DRD, which is generally available to corporate shareholders. No assurance can be given that we will have sufficient earnings and profits (as determined for U.S. federal income tax purposes) to cause any distributions to be eligible for a DRD. In addition, a DRD is available only if certain holding periods and other taxable income requirements are satisfied.

Sale of Common Stock

A U.S. holder of common stock will generally recognize gain or loss on the taxable sale, exchange or other taxable disposition of such stock in an amount equal to the difference between such U.S. holder’s amount realized on the sale

Table of Contents

and its adjusted tax basis in the common stock sold. A U.S. holder's basis in common stock is generally the cost of the stock less any distributions that are treated as return of capital (as described above). Special rules apply for determining the basis of stock acquired as a gift or by inheritance. A U.S. holder's amount realized should equal the amount of cash and the fair market value of any property received in consideration of its stock. The gain or loss should be capital gain or loss and should be long-term capital gain or loss if the common stock is held for more than one year at the time of disposition. The deductibility of capital losses for U.S. federal income tax purposes is subject to limitations under the Code. Under current law, long-term capital gain recognized by an individual U.S. holder is generally eligible for a preferential U.S. federal income tax rate.

Information Reporting and Backup Withholding

Information reporting requirements generally will apply to payments of dividends on shares of common stock and to the proceeds of a sale of common stock unless a U.S. holder is an exempt recipient, such as a corporation. Backup withholding will apply to those payments if a U.S. holder fails to provide its correct taxpayer identification number or fails to report full dividend income. Any amount withheld under the backup withholding rules will be allowed as a refund or a credit against U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Certain U.S. Federal Income Tax Considerations for Non-U.S. Holders of Common Stock

Dividends on our Common Stock

We do not expect to declare or pay any distributions on our common stock in the foreseeable future. If we do make any distributions on shares of our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Distributions in excess of our current and accumulated earnings and profits will constitute a return of capital that is applied against and reduces, but not below zero, a non-U.S. holder's adjusted tax basis in shares of our common stock. Any remaining excess will be treated as gain realized on the sale or other disposition of our common stock. See "Sale of Common Stock." Any dividend paid to a non-U.S. holder on our common stock will generally be subject to U.S. withholding tax at a 30% rate. The withholding tax might not apply, however, or might apply at a reduced rate, under the terms of an applicable income tax treaty between the United States and the non-U.S. holder's country of residence. Non-U.S. holders should consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty. Generally, for us or our paying agent to withhold tax at a lower treaty rate, a non-U.S. holder must certify its entitlement to treaty benefits. A non-U.S. holder generally can meet this certification requirement by providing to us or our paying agent an applicable IRS form in the W-8 series (which generally remains valid for three years, after which time a new properly completed and executed form must be provided to us or our paying agent). If the holder holds the stock through a financial institution or other agent acting on the holder's behalf, the holder will be required to provide appropriate documentation to the agent. The holder's agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. If a non-U.S. holder is eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty, the non-U.S. holder may obtain a refund or credit of any excess amounts withheld by filing an appropriate claim for a refund with the IRS in a timely manner.

Dividends received by a non-U.S. holder that are effectively connected with a U.S. trade or business conducted by the non-U.S. holder, or, if an income tax treaty between the United States and the non-U.S. holder's country of residence applies, are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder in the United States, are not subject to such withholding tax. To obtain this exemption, a non-U.S. holder must provide us or our paying agent with an IRS Form W-8ECI properly certifying such exemption. Such effectively connected dividends, although not subject to withholding tax, are taxed at the same graduated rates applicable to U.S. persons, as defined

under the Code, net of certain deductions and credits, subject to any applicable income tax treaty providing otherwise. In addition to the graduated tax described above, dividends received by corporate non-U.S. holders that are effectively connected with a U.S. trade or business of the corporate non-U.S. holder may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty.

S-16

Table of Contents

Sale of Common Stock

Non-U.S. holders will generally not be subject to U.S. federal income tax on any gains realized on the sale, exchange or other disposition of common stock unless:

- the gain (1) is effectively connected with the conduct by the non-U.S. holder of a U.S. trade or business and (2) if an income tax treaty between the United States and the non-U.S. holder's country of residence applies, the gain is attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder in the United States, in which case the special rules described below apply;
- the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of the sale, exchange or other disposition of our common stock, and certain other requirements are met, in which case the gain would be subject to a flat 30% tax, or such reduced rate as may be specified by an applicable income tax treaty, which may be offset by U. S. source capital losses, even though the individual is not considered a resident of the United States; or
- if we are, or were within the shorter of the five-year period preceding the disposition and the non-U.S. holder's holding period, a "U.S. real property holding corporation," or USRPHC.

We do not believe that we are a USRPHC and we do not anticipate becoming one in the future. If we are or become a USRPHC, as long as our common stock is regularly traded on an established securities market, only a non-U.S. holder that actually or constructively owns (at any time during the shorter of the five-year period preceding the date of disposition or the holder's holding period) more than 5% of our outstanding common stock will be subject to U.S. federal income tax on the disposition of our common stock.

Any gain described in the first bullet point above will be subject to U.S. federal income tax at the regular individual or corporate income tax rates. If the non-U.S. holder is a corporation, under certain circumstances, that portion of its earnings and profits that is effectively connected with its U.S. trade or business, subject to certain adjustments, will be subject to a "branch profits tax." The branch profits tax rate is generally 30%, although an applicable income tax treaty between the United States and the non-U.S. holder's country of residence may provide for a lower rate.

Information Reporting and Backup Withholding

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in "Dividends on Our Common Stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an

additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or

S-17

Table of Contents

credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding on Foreign Accounts

Legislation known as the Foreign Account Tax Compliance Act and guidance issued thereunder ("FATCA") imposes withholding taxes on certain types of payments made to "foreign financial institutions" and certain other foreign entities (including financial intermediaries). FATCA generally imposes withholding at a rate of 30% on payments to certain foreign entities of dividends on our common stock and the gross proceeds of dispositions of our common stock, unless various U.S. information reporting and due diligence requirements (generally relating to ownership by U.S. persons of interests in or accounts with those entities) have been satisfied or the entity otherwise qualifies for an exemption. An intergovernmental agreement between the United States and an applicable foreign country may modify these requirements. The required withholding currently applies to dividends on our common stock. The U.S. Treasury Department and the IRS had previously announced that withholding on payments of gross proceeds from a sale or other disposition of certain financial instruments treated as providing for U.S.-source dividends (such as the common stock) or interest would only apply to payments beginning on January 1, 2019. However, under recently proposed regulations (the preamble to which specifies that taxpayers are permitted to rely on those proposed regulations pending finalization), no withholding will apply on payments of gross proceeds. You should consult your tax advisor regarding the application of FATCA.

U.S. Federal Estate Tax

An individual Non-U.S. Holder who is treated as the owner of, or has made certain lifetime transfers of, an interest in our common stock will be required to include the value thereof in his or her gross estate for U.S. federal estate tax purposes, and may be subject to U.S. federal estate tax unless an applicable estate tax treaty provides otherwise, even though such individual was not a citizen or resident of the United States at the time of his or her death.

The preceding discussion of U.S. federal tax considerations is for general information only. It is not tax advice. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

Table of Contents

PLAN OF DISTRIBUTION

We have entered into an Equity Distribution Agreement with Canaccord under which we may issue and sell from time to time up to \$24,650,000 of our common stock through Canaccord as our sales agent. The Equity Distribution Agreement was filed as an exhibit to a Current Report on Form 8-K filed with the SEC on April 12, 2019. Sales of the common stock, if any, will be made at market prices by methods deemed to be an “at the market” offering as defined in Rule 415 promulgated under the Securities Act, including sales made directly on the New York Stock Exchange American market, on any other existing trading market for the common stock, or to or through a market maker other than on an exchange. Canaccord may also sell our common stock hereunder by any other method permitted by law, including in privately negotiated transactions.

Upon delivery of a placement notice, Canaccord may offer the common stock subject to the terms and conditions of the Equity Distribution Agreement on a daily basis or as otherwise agreed upon by us and Canaccord. We will designate the maximum amount of common stock to be sold through Canaccord on a daily basis or otherwise determine such maximum amount together with Canaccord. Subject to the terms and conditions of the Equity Distribution Agreement, Canaccord 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 Canaccord 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 Canaccord may suspend the offering of the common stock being made through Canaccord under the Equity Distribution Agreement upon proper notice to the other party and subject to other conditions.

We will pay Canaccord commissions, in cash, for its services in acting as agent in the sale of our common stock. The aggregate compensation payable to Canaccord as sales agent shall be equal to 3% of the gross sales price per share of all shares sold through it as agent under the Equity Distribution Agreement. 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. In addition, we have agreed to reimburse a portion of the expenses of Canaccord in connection with this offering up to a maximum of \$50,000, as well as Canaccord’s FINRA counsel fees in an amount up to \$10,000. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Canaccord under the Equity Distribution Agreement, will be approximately \$140,000.

Settlement for sales of common stock will occur on the second business day following the date on which any sales are made, or on some other date that is agreed upon by us and Canaccord in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Canaccord may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Canaccord will use its commercially reasonable efforts, consistent with its sales and trading practices, to solicit offers to purchase the common stock shares under the terms and subject to the conditions set forth in the Equity Distribution Agreement. In connection with the sales of the common stock on our behalf, Canaccord may be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation to Canaccord will be deemed to be underwriting commissions or discounts. We have also agreed in the Equity Distribution Agreement to provide indemnification and contribution to Canaccord with respect to certain liabilities, including liabilities under the Securities Act.

The offering of our common stock pursuant to Equity Distribution Agreement will terminate automatically upon the sale of all shares of our common stock subject to the Equity Distribution Agreement or as otherwise permitted therein. We and Canaccord may each terminate the Equity Distribution Agreement at any time upon ten days’ prior written notice.

Any portion of the \$24,650,000 included in this prospectus supplement that is not previously sold or included in an active placement notice pursuant to the Equity Distribution Agreement is available for sale in other offerings pursuant to the accompanying base prospectus, and if no shares are sold under the Equity Distribution Agreement, the full \$24,650,000 of securities may be sold in other offerings pursuant to the accompanying base prospectus.

S-19

Table of Contents

Our common stock is listed on the New York Stock Exchange American market under the trading symbol “AMPE.” The transfer agent for our common stock is Corporate Stock Transfer, Inc.

Canaccord and its affiliates may in the future provide various investment banking, commercial banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M, Canaccord will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus supplement.

This prospectus supplement and the accompanying prospectus in electronic format may be made available on a website maintained by Canaccord and Canaccord may distribute this prospectus supplement and the accompanying prospectus electronically.

S-20

Table of Contents

DESCRIPTION OF CAPITAL STOCK

General

Our authorized capital stock consists of 200,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of undesignated preferred stock, \$0.0001 par value, of which no preferred shares are issued or outstanding.

The following summary description of our capital stock is based on the provisions of our certificate of incorporation and bylaws and the applicable provisions of the Delaware General Corporation Law. This information is qualified entirely by reference to the applicable provisions of our certificate of incorporation, bylaws and the Delaware General Corporation Law. For information on how to obtain copies of our certificate of incorporation and bylaws, please see “Where You Can Find Additional Information” and “Incorporation of Certain Information by Reference.”

S-21

Table of Contents

LEGAL MATTERS

The validity of the securities offered by this prospectus supplement will be passed on for us by Squire Patton Boggs (US) LLP. Certain legal matters in connection with this offering will be passed on for Canaccord by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.

EXPERTS

The audited financial statements incorporated by reference in this prospectus supplement and elsewhere in the registration statement have been so incorporated by reference in reliance upon the report of Plante & Moran PLLC, independent registered public accountants, upon the authority of said firm as experts in accounting and auditing.

S-22

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 (File No. 333-217094), of which this prospectus supplement and the accompanying base prospectus are a part, under the Securities Act, to register the shares of common stock offered by this prospectus supplement. However, this prospectus supplement and the accompanying base prospectus do not contain all of the information contained in the registration statement and the exhibits and schedules to the registration statement. We encourage you to carefully read the registration statement and the exhibits and schedules to the registration statement.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings can be read and copied at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. The public may obtain information on the operation of the public reference room by calling the SEC at 1-800-SEC-0330. Also, the SEC maintains a website at www.sec.gov that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC, including us.

Our common stock is listed on the New York Stock Exchange American market under the symbol "AMPE." General information about our company, including our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as any amendments and exhibits to those reports, are available free of charge through our website at www.ampiopharma.com as soon as reasonably practicable after we file them with, or furnish them to, the SEC. Information on, or that can be accessed through, our website is not incorporated into this prospectus supplement or other securities filings and is not a part of these filings.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

We "incorporate by reference" into this prospectus supplement the information we file with the SEC, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus supplement and information that we file subsequently with the SEC will automatically update this prospectus supplement. We incorporate by reference the documents listed below and any filings we make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Securities Exchange Act of 1934, as amended, after initial filing of the registration statement that contains the prospectus and prior to the time that we sell all the securities offered by this prospectus supplement (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, 2018 filed with the SEC on March 18, 2019;
- our Proxy Statement on Schedule 14A filed with the SEC on October 31, 2018 (excluding those portions that are not incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2017);
- our Current Report on Form 8-K filed on April 12, 2019; and
- the description of our common stock contained or incorporated by reference in our Registration Statement on Form 8-A, filed on May 17, 2011, including any amendment or reports filed for the purpose of updating this description.

You may request a copy of these filings (other than an exhibit to a filing unless that exhibit is specifically incorporated by reference into that filing) at no cost, by writing to or telephoning us at the following address:

Ampio Pharmaceuticals, Inc.

373 Inverness Parkway, Suite 200

Englewood, Colorado 80112

(720) 437 6500

Attn: Investor Relations

S-23

Table of Contents

PROSPECTUS

\$100,000,000

Common Stock

Preferred Stock

Debt Securities

Warrants

Units

5,000,000 Shares of Common Stock Offered by

the Selling Stockholder

Issuable Upon Exercise of Warrants

We may, from time to time, offer and sell up to \$100,000,000 of any combination of our common stock, preferred stock, debt securities or warrants described in this prospectus, either individually or in combination with other securities, at prices and on terms described in one or more supplements to this prospectus. We may also offer common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock, or common stock, preferred stock or debt securities upon the exercise of warrants. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings.

In addition, the selling stockholder may from time to time, offer and sell up to 5,000,000 shares our common stock issuable upon the exercise of warrants held by such selling stockholder. We will not receive any of the proceeds from the sales of common stock from the selling stockholder, however, the selling stockholder would pay us the exercise price of \$0.40 per, for an aggregate amount of \$2,000,000 if the warrants are exercised for cash, in full, subject to any adjustments. See “Use of Proceeds.” The selling stockholder may sell the shares of common stock described in this prospectus in a number of different ways and at varying prices. See “Plan of Distribution” below for additional information on how the selling stockholder may conduct sales of our common stock. We have agreed to bear the expenses of the registration of the common stock under the federal and state securities laws on behalf of the selling stockholder.

Each time we offer securities, 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 also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before buying any of the securities being offered.

The securities offered by this prospectus may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers. We will set forth the names of any underwriters or agents and any applicable fees, commissions, discounts and over-allotments in an accompanying prospectus supplement. For additional information on the methods of sale, you should refer to the section entitled “Plan of Distribution” in this prospectus and in the applicable 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.

Our common stock is traded on the NYSE MKT LLC under the symbol “AMPE.” On March 29, 2017, the last reported sale price of our common stock on the NYSE MKT LLC was \$0.80. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on the NYSE MKT LLC or any securities market or other exchange of the securities covered by the applicable prospectus supplement.

Table of Contents

This prospectus may not be used to offer or sell any securities unless accompanied by a prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties referenced under the heading “risk factors” on page 5 of this prospectus as well as those contained in the applicable prospectus supplement and any related free writing prospectus, and in the other documents that are incorporated by reference into this prospectus.

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 April 20, 2017.

Table of Contents

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	Page 1
<u>SUMMARY</u>	1
<u>RISK FACTORS</u>	5
<u>FORWARD-LOOKING STATEMENTS</u>	5
<u>RATIO OF EARNINGS TO COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS</u>	7
<u>USE OF PROCEEDS</u>	8
<u>SELLING STOCKHOLDERS</u>	9
<u>PLAN OF DISTRIBUTION</u>	11
<u>DESCRIPTION OF CAPITAL STOCK</u>	14
<u>DESCRIPTION OF DEBT SECURITIES</u>	19
<u>DESCRIPTION OF WARRANTS</u>	26
<u>DESCRIPTION OF UNITS</u>	27
<u>LEGAL MATTERS</u>	28
<u>EXPERTS</u>	28
<u>WHERE YOU CAN FIND ADDITIONAL INFORMATION</u>	28
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	28

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, utilizing a “shelf” registration process. Under this shelf registration process, we may offer shares of our common stock preferred stock, debt securities, and/or warrants to purchase our common stock, either individually or in units, in one or more offerings, up to a total dollar amount of \$100,000,000. In addition, the selling stockholder may sell up to an aggregate of 5,000,000 shares of our common stock issuable upon the exercise of warrants held by such selling stockholder. This prospectus provides you with a general description of the securities we and the selling stockholder may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the specific terms of the 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. Each such 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 incorporated by reference into this prospectus. We urge you to carefully read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the headings “Where You Can Find Additional Information” and “Incorporation of Certain Information by Reference” before buying any of the securities being offered. This prospectus may not be used to offer or sell securities unless it is accompanied by a prospectus supplement.

You should rely only on the information contained or incorporated by reference in this prospectus, any applicable prospectus supplement and any related free writing prospectus. We have not authorized anyone to provide you with different information in addition to or different from that contained in this prospectus, any applicable prospectus supplement and any related free writing prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we may authorize to be provided to you. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading “Where You Can Find Additional Information.”

SUMMARY

This summary highlights selected information from this prospectus or incorporated by reference in 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, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities contained in the applicable prospectus supplement and any related free writing prospectus, and in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Unless otherwise indicated or unless the context otherwise requires, references in this prospectus to the “Company,” “Ampio,” “we,” “us,” or “our” are to Ampio Pharmaceuticals, Inc. and its subsidiaries.

Table of Contents

Overview

We are a biopharmaceutical company focused primarily on the development of therapies to treat prevalent inflammatory conditions for which there are limited treatment options.

Our product portfolio is primarily based on the work of Dr. David Bar-Or, the Director of Trauma Research LLC for the Swedish Medical Center located in Englewood, CO, St. Anthony Hospital located in Lakewood, CO and the medical center of Plano located in Plano, Texas. For over two decades, while directing these trauma research laboratories, Dr. Bar-Or and his staff have built a robust portfolio of product candidates focusing on inflammatory conditions. Our initial clinical programs were selected from Dr. Bar-Or's research based on certain criteria, particularly the ability to advance the candidates rapidly into late-stage clinical trials. The benchmarks used to build our pipeline were products with: (i) potential indications to address large underserved markets; (ii) strong intellectual property protection and the potential for market and data exclusivity; and (iii) a well-defined regulatory path to marketing approval.

We are primarily developing compounds that decrease inflammation by (i) inhibiting specific pro-inflammatory compounds by affecting specific pathways at the protein expression and at the transcription level; (ii) activating specific phosphatase or depleting available phosphate needed for the inflammation process; and (iii) decreasing vascular permeability.

Our predecessor, DMI Life Sciences, Inc., or Life Sciences, was incorporated in Delaware in December 2008. In March 2010, Life Sciences was merged with a subsidiary of Chay Enterprises, Inc. As a result of this merger, Life Sciences stockholders became the controlling stockholders of Chay Enterprises. Following the merger, we reincorporated in Delaware as Ampio Pharmaceuticals, Inc. in March 2010.

Corporate Information

Our principal executive offices are located at 373 Inverness Parkway, Suite 200, Englewood, Colorado 80112, and our telephone number is (720) 437 6500. Additional information about us is available on our website at www.ampiopharma.com. The information contained on or that may be obtained from our website is not, and shall not be deemed to be, a part of this prospectus. You can review filings we make with the SEC at its website (www.sec.gov), including our annual reports on Form 10 K, quarterly reports on Form 10 Q, current reports on Form 8 K and amendments to those reports electronically filed or furnished pursuant to Section 15(d) of the Exchange Act.

The Securities We May Offer

We may offer shares of our common stock, various series of preferred stock, debt securities and/or warrants to purchase our common stock, either individually or in units, with a total value of up to \$100,000,000 from time to time under this prospectus at prices and on terms to be determined at the time of any offering. In addition, the selling stockholder may sell up to an aggregate of 5,000,000 shares of our common stock issuable upon the exercise of warrants held by such selling stockholder. This prospectus provides you with a general description of the securities we and the selling stockholder may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or offering price;
- maturity, if applicable;

- original issue discount, if any;
- rates and times of payment of interest or dividends, if any;

Table of Contents

- 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;
- restrictive covenants, if any; and
- voting or other rights, if any.

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.

This prospectus may not be used to offer or sell securities unless it is accompanied by a prospectus supplement.

We and the selling stockholder may sell the securities directly to investors or to or through agents, underwriters or dealers. We and the selling stockholder, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we or the selling stockholder does offer securities to or through agents or underwriters, we will include in the applicable prospectus supplement:

- the names of those agents or underwriters;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time and the selling stockholder may offer up to 5,000,000 shares of common stock issuable upon exercise of warrants held by such selling stockholder. Holders of shares of our common stock are entitled to one vote for each share held of record on all matters to be voted on by stockholders and do not have cumulative voting rights. Subject to the preferences that may be applicable to any then outstanding preferred stock, the holders of our outstanding shares of common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds. In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Under our certificate of incorporation, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or the rules of any stock exchange or market on which our securities are then traded), to designate up to 10,000,000 shares of preferred stock in one or more series and to determine the designations, voting powers, preferences and rights of each series of the preferred stock, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series, any or all of which may be greater than the rights of the common stock. Any convertible preferred stock we may issue will be convertible into our common stock or exchangeable for our other securities. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of such series of preferred stock, as well as the qualifications, limitations or restrictions thereof, in the

Table of Contents

certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. We urge you to read the applicable 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 issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into or exchangeable for our common stock or preferred stock. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

The debt securities will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete 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 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.

Warrants. We may issue warrants for the purchase of common stock in one or more series. We may issue warrants independently or together with common stock, and the warrants may be attached to or separate from our common stock. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the complete warrant agreements and/or warrant certificates that contain the terms of the warrants. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the forms of warrant agreement and/or warrant certificates that describe the terms of the series of warrants we are offering before the issuance of the related series of warrants.

We will evidence each series of warrants by warrant certificates that we will issue. Warrants may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

Units. We may issue, in one or more series, units consisting of common stock and/or warrants for the purchase of common stock 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. In this prospectus, we have summarized certain general features of the units. We urge you, however, to read the applicable 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 agreement, if any, that contains the terms of the units. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, any form of unit agreement and any supplemental agreements that describe the terms of the series of units we are offering before the issuance of the related series of units.

Table of Contents

RISK FACTORS

Investing in our securities involves risks. You should carefully consider the risk factors contained in the applicable prospectus supplement and any related free writing prospectus for a specific offering of securities, as well as those incorporated by reference in this prospectus, before making an investment decision. You should also carefully consider other information contained and incorporated by reference in this prospectus and any applicable prospectus supplement, including our financial statements and the related notes thereto incorporated by reference in this prospectus. The risks and uncertainties described in the applicable prospectus supplement and our other filings with the SEC incorporated by reference herein are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently consider immaterial may also adversely affect us. If any of the described risks occur, our business, financial condition or results of operations could be materially harmed. In such case, the value of our securities could decline and you may lose all or part of your investment.

FORWARD-LOOKING STATEMENTS

This prospectus, the documents incorporated by reference herein contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Forward-looking statements are those that predict or describe future events or trends and that do not relate solely to historical matters. You can generally identify forward-looking statements as statements containing the words “believe,” “expect,” “may,” “will,” “anticipate,” “intend,” “estimate,” “project,” “plan,” “assume” or other similar expressions, although not all forward-looking statements contain these identifying words. All statements contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein regarding our future strategy, plans and expectations regarding clinical trials, future regulatory approvals, our plans for the manufacturing and commercialization of our products, future operations, projected financial position, potential future revenues, projected costs, future prospects, and results that might be obtained by pursuing management’s current plans and objectives are forward-looking statements. Forward-looking statements include, but are not necessarily limited to, those relating to:

- our need for, and ability to raise, additional capital;
- the results and timing of our clinical trials;
- the regulatory review process and any regulatory approvals that may be issued or denied by the Food and Drug Administration, the European Medicines Agency, or other regulatory agencies;
- our manufacturing plans;
- our need to secure collaborators to license, manufacture, market and sell any products for which we receive regulatory approval in the future;
- the results of our internal research and development efforts; the commercial success and market acceptance of any of our product candidates that are approved for marketing in the United States or other countries;
- the safety and efficacy of medicines or treatments introduced by competitors that are targeted to indications which our product candidates have been developed to treat;
- the acceptance and approval of regulatory filings;
- our current or prospective collaborators’ compliance or non-compliance with their obligations under our agreements with them, or decisions by our collaborators to discontinue clinical trials and return product candidates to us;
- our plans to develop other product candidates; and

Table of Contents

· other factors discussed elsewhere in this prospectus or the documents incorporated by reference herein.

You should not place undue reliance on our forward-looking statements because the matters they describe are subject to known and unknown risks, uncertainties and other unpredictable factors, many of which are beyond our control. Our forward-looking statements are based on the information currently available to us and speak only as of the date on the cover of this prospectus. New risks and uncertainties arise from time to time, and it is impossible for us to predict these matters or how they may affect us. We have included important factors in the cautionary forward-looking statements included in this prospectus, particularly in the section of this prospectus entitled “Risk Factors,” which we believe over time, could cause our actual results, performance or achievements to differ from the anticipated results, performance or achievements that are expressed or implied by our forward-looking statements. We have no duty to, and do not intend to, update or revise the forward-looking statements in this prospectus after the date of this prospectus except to the extent required by the federal securities laws. You should consider all risks and uncertainties disclosed in our filings with the Securities and Exchange Commission, or the SEC, described in the sections of this prospectus entitled “Where You Can Find More Information” and “Incorporation of Certain Information by Reference,” all of which are accessible on the SEC’s website at www.sec.gov.

Table of Contents

RATIO OF EARNINGS TO COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS

The following table sets forth our ratio of earnings to fixed charges and the ratio of earnings to combined fixed charges and preference securities dividends for each of the periods indicated. The following table is qualified by the more detailed information appearing in the computation table set forth in Exhibit 12.1 to the registration statement of which this prospectus is part and our historical financial statements, including the notes to those financial statements, incorporated by reference in this prospectus.

	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
Ratio of earnings to combined fixed charges and preferred stock dividends	deficiency	deficiency	deficiency	deficiency	deficiency
Deficiency (in thousands)					
(\$)	\$ 19,163	\$ 32,010	\$ 38,125	\$ 24,009	\$ 11,593

For these purposes, earnings are defined as income before income taxes and fixed charges, and fixed charges include interest expense on indebtedness, amortization of capitalized interest, and the portion of operating lease rental expense which is deemed to represent interest. The deficiency is calculated before the loss attributable to non-controlling interests and is disclosed for periods in which net losses were insufficient to cover fixed charges.

Table of Contents

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered by us hereby. Except as described in any prospectus supplement or any related free writing prospectus that we may authorize to be provided to you, we currently intend to use the net proceeds from the sale of the securities offered by us hereby for general corporate purposes, which may include capital expenditures, working capital and general and administrative expenses. We will set forth in the applicable prospectus supplement or free writing prospectus our intended use for the net proceeds received from the sale of any securities sold pursuant to the prospectus supplement or free writing prospectus. Pending these uses, we intend to invest the net proceeds in short-term obligations of the U.S. government and its agencies.

We will not receive any proceeds from the sale by the selling stockholder of the common stock underlying the warrants covered by this prospectus. However, upon exercise of the warrants for cash, the selling stockholder would pay us the applicable exercise price of \$0.40 per share, or an aggregate of \$2,000,000 if the warrants are exercised for cash in full, subject to certain adjustments in the event of a major transaction, as defined in the warrants. Under certain conditions set forth in the warrants, the warrants are exercisable on a cashless basis. If the warrants are exercised on a cashless basis, we would not receive any cash payment from the selling stockholder upon exercise of the warrants.

Table of Contents

SELLING STOCKHOLDER

This prospectus also relates to the possible resale by certain of our stockholder, who we refer to in this prospectus as the “selling stockholder,” of up to 5,000,000 shares of our common stock that are issuable, upon exercise of certain warrants, prior to the original date of filing of the registration statement of which this prospectus forms a part. On August 29, 2016, we (i) entered into a Securities Purchase Agreement (the “Securities Purchase Agreement”) with CVI Investments, Inc. (“CVI”), pursuant to which we issued 5,000,000 shares of our common stock, \$0.0001 par value per share (the “Common Stock”), together with warrants (the “CVI Warrants”) to purchase up to 5,000,000 shares of Common Stock with an exercise price of \$1.00 per share (the “CVI Warrant Exercise Price”) at a combined offering price of \$0.75 per share of Common Stock and accompanying Warrant on September 1, 2016 (the “Offering”).

The Warrants became exercisable immediately upon issuance and from time to time thereafter through and including the fifth year anniversary of the initial exercise date. The Warrants prohibit any exercise by a holder that would cause such holder to hold in excess of 4.99% of our then issued and outstanding shares of Common Stock. This limitation may be increased to 9.99% of our then issued and outstanding shares of Common Stock upon 61 days’ prior written notice from a Warrant holder. The exercise price of the Warrants was subject to adjustment in the event we issued securities, other than certain permitted issuances, at a per share price less than the exercise price of the Warrants. In the event of a change of control of the Company, the holder of the CVI Warrants may demand redemption of the CVI Warrants for cash in accordance with a Black-Scholes option pricing model. As long as any CVI Warrants remained outstanding, we were not able to issue any options or securities convertible into shares of our Common Stock at a variable price.

On March 27, 2017, we entered into a Waiver and Consent Letter Agreement (the “Waiver and Consent Agreement”) with CVI, amending the terms of the CVI Warrants. Under the Waiver and Consent Agreement, CVI waived the right to have the CVI Warrant Exercise Price reduced and the number of shares of Common Stock underlying the CVI Warrants increased in the event we secure any financing, including debt, which includes issuing or selling shares of Common Stock for a price per share less than the CVI Warrant Exercise Price. CVI also waived the prohibition on the our ability to issue or sell shares of its Common Stock, options or convertible securities at a price which varies or may vary with the market price of the Common Stock or pursuant to an equity credit line or similar “at the market” offering. The waivers are permanent. In return, we have agreed to reduce the exercise price of the CVI Warrants from \$1.00 per share of Common Stock to \$0.40 per share of Common Stock and to not issue or sell any shares of our capital stock for a period of 10 trading days following the execution of the Waiver and Consent Agreement. All other terms of the CVI Warrants remain the same.

The following table sets forth the name of the selling stockholder, the total number of shares of common stock beneficially owned by the selling stockholder prior to this offering, the percentage that the selling stockholder beneficially owned prior to this offering, the number of shares of common stock covered by this prospectus and the total number of shares of common stock and percentage that the selling stockholder will beneficially own upon completion of this offering. Beneficial ownership is determined in accordance with SEC rules. The information is not necessarily indicative of beneficial ownership for any other purpose. In general, under these rules a beneficial owner of a security includes any person who, directly or indirectly, through any contract, arrangement, understanding, relationship or otherwise has or shares voting power or investment power with respect to such security. A person is also deemed to be a beneficial owner of a security if that person has the right to acquire beneficial ownership of such security within 60 days. The amounts set forth below are based upon information provided to us by representatives of the selling stockholder, or on our records, and are accurate to the best of our knowledge as of the date specified below. To our knowledge, except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock beneficially owned by that person.

The number of shares of common stock outstanding and percentage of beneficial ownership before this offering set forth below is computed on the basis of 57,242,164 shares of our common stock issued and outstanding as of March 15, 2017. The number of shares of common stock and percentage of beneficial ownership after the consummation of this offering set forth below are based on the number of shares to be issued and outstanding immediately after the consummation of this offering. Shares of our common stock that a person has the right to acquire within 60 days of the date of this prospectus are deemed outstanding for purposes of computing the percentage ownership of such person's holdings, but are not deemed outstanding for purposes of computing the percentage ownership of any other person.

Table of Contents

We do not know when or in what amounts the selling stockholder may sell or otherwise dispose of the shares covered hereby. The selling stockholder might not sell any or all of the shares covered by this prospectus or may sell or dispose of some or all of their shares in transactions exempt from the registration requirements of the Securities Act, or in the open market after the date on which they provided the information set forth in the table below. Because the selling stockholder may not sell or otherwise dispose of some or all of the shares covered by this prospectus and because there are currently no agreements, arrangements or understandings with respect to the sale or other disposition of any of the shares, we cannot estimate the number of the shares that will be held by the selling stockholder after completion of a potential offering. For purposes of the table below, we have assumed that the selling stockholder will have sold all of the shares covered by this prospectus upon completion of the applicable offering.

	Common stock beneficially owned		Maximum number of shares that may be offered pursuant to this prospectus	Shares of common stock beneficially owned after Giving effect to this offering(3)	
	Shares of common stock beneficially owned prior to this offering(1) (2)			Number	Percentage
	Number	Percentage			
CVI Investments, Inc. (4)	5,000,000	8.0%	5,000,000	—	—
Total	5,000,000	8.0%	5,000,000	—	—

* Less than one percent (1%).

- (1) Represents the number of shares of common stock that may be issued upon exercise of the warrants. For the purposes hereof, we assume the issuance of all such shares pursuant to a cash exercise. The actual number of shares of common stock issuable upon exercise of the warrants is subject to adjustment for any stock split, stock dividend or similar transaction involving the common stock, and could be materially less or more than such number depending on factors which cannot be predicted by us at this time. The actual number of shares of common stock described in this prospectus, and included in the registration statement of which this prospectus is a part, includes such additional number of shares of common stock as may be issued or issuable upon exercise of the warrants by reason of any stock split, stock dividend or similar transaction involving the common stock, in accordance with Rule 416 under the Securities Act.
- (2) The terms of the warrant held by the selling stockholder contains warrants prohibit any exercise that would cause such holder to hold in excess of 4.99% of our then issued and outstanding shares of common stock. This limitation may be increased to 9.99% of our then issued and outstanding shares of common stock upon 61 days' prior written notice from CVI.
- (3) Assumes that the selling stockholder will sell all shares of common stock offered by it under this prospectus.
- (4) Consists of 5,000,000 shares of common stock issuable upon exercise of warrants. Heights Capital Management, Inc. is the investment manager to CVI Investments, Inc. and as such may exercise voting and dispositive power over these shares. The principal business address of CVI Investments, Inc. is P.O. Box 309GT, Uglund House, South Church Street, George Town, Grand Cayman, KY 1 1104, Cayman Islands.

Table of Contents

PLAN OF DISTRIBUTION

Ampio's Plan of Distribution

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. The securities may be distributed from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
 - at prices related to such prevailing market prices; or
- at negotiated prices.

Each time we offer and sell securities hereto, we will provide a prospectus supplement that will set forth the terms of the offering of the securities, including:

- the name or names of the underwriters, if any;
- the purchase price of the securities and the proceeds we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- any public offering price;
- any discounts or concessions allowed or re-allowed or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the 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. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. Any public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. The prospectus supplement, naming the underwriter, will describe the nature of any such relationship.

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

We may authorize agents or underwriters to solicit offers by certain purchasers to purchase 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 prospectus supplement will set forth the conditions to these contracts and any commissions we must pay for solicitation of these contracts.

Table of Contents

We may provide agents and underwriters with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

Any warrants we may offer will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment 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 price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or 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 stabilizing or 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 the activities at any time.

Any underwriters that are qualified market makers on the NYSE MKT LLC may engage in passive market making transactions in the common stock on the NYSE MKT LLC in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. 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. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

Selling Stockholder's Plan of Distribution

We are registering the shares of common stock issuable upon exercise of the warrants held by the selling stockholder to permit the resale of these shares from time to time after the date of this prospectus. We will not receive any proceeds from the sale by the selling stockholder of the common stock underlying the warrants covered by this prospectus. However, upon exercise of the warrants for cash, the selling stockholder would pay us the applicable exercise price of \$0.40 per share, or an aggregate of \$2,000,000 if the warrants are exercised for cash in full, subject to certain adjustments in the event of a major transaction, as defined in the warrants. Under certain conditions set forth in the warrants, the warrants are exercisable on a cashless basis. If the warrants are exercised on a cashless basis, we would not receive any cash payment from the selling stockholder upon exercise of the warrants.

The selling stockholder may sell all or a portion of the shares of common stock beneficially owned by it upon exercise of the warrants and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If the shares of common stock are sold through underwriters or broker-dealers, the selling stockholder will be responsible for underwriting discounts or commissions or agent's commissions. The shares of common stock may be sold in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale or at negotiated prices. These sales may be effected from time to time pursuant to one or more of the following methods, which may involve crosses or block transactions:

on any national securities exchange or U.S. inter-dealer quotation system of a registered national securities association on which the securities may be listed or quoted at the time of sale;

- in the over-the-counter market;
- in transactions otherwise than on these exchanges or systems or in the over-the-counter market;

Table of Contents

- through the writing or settlement of options or other hedging transactions, whether such options are listed on an options exchange or otherwise;
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
 - an exchange distribution in accordance with the rules of the applicable exchange;
- public or privately negotiated transactions;
- through the settlement of short sales;
- transactions in which broker-dealers agree with the selling stockholder to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

If the selling stockholder effects such transactions by selling shares of common stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling stockholder or commissions from purchasers of the shares of common stock for whom they may act as agent or to whom they may sell as principal (which discounts, concessions or commissions as to particular underwriters, broker-dealers or agents may be in excess of those customary in the types of transactions involved). In connection with sales of the shares of common stock or otherwise, the selling stockholder may enter into hedging transactions with broker-dealers, which may in turn engage in short sales of the shares of common stock in the course of hedging in positions they assume. The selling stockholder may also sell shares of common stock short and deliver shares of common stock covered by this prospectus to close out short positions, and to return borrowed shares in connection with such short sales, provided that the short sales are made after the registration statement of which this prospectus forms a part is declared effective. The selling stockholder may also loan or pledge shares of common stock to broker-dealers in connection with bona fide margin accounts secured by the shares of common stock, which shares broker-dealers could in turn sell if the selling stockholder defaults in the performance of its respective secured obligations.

The selling stockholder may pledge or grant a security interest in some or all of the shares of common stock owned by it and, if it defaults in the performance of its secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time pursuant to this prospectus. The selling stockholder also may transfer and donate the shares of common stock in other circumstances in which case the transferees, donees or other successors in interest will be the selling beneficial owners for purposes of this prospectus. We will file an amendment or supplement to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act of 1933, amending, if necessary, the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

The selling stockholder and any broker-dealer participating in the distribution of the shares of common stock may be deemed to be “underwriters” within the meaning of the Securities Act of 1933, and any commission paid, or any discounts or concessions allowed to, any such broker-dealer may be deemed to be underwriting commissions or discounts under the Securities Act of 1933. At the time a particular offering of the shares of common stock is made, a prospectus supplement, if required, will be distributed which will set forth the aggregate amount of shares of common stock being offered and the terms of the offering, including the name or names of any underwriters, broker-dealers or

Table of Contents

agents, any discounts, commissions and other terms constituting compensation from the selling stockholder and any discounts, commissions or concessions allowed or reallocated or paid to underwriters or broker-dealers.

Under the securities laws of some states, the shares of common stock may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states the shares of common stock may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with.

There can be no assurance that the selling stockholder will sell any or all of the shares of common stock underlying the warrants registered pursuant to the registration statement of which this prospectus forms a part.

The selling stockholder and any other person participating in such distribution will be subject to applicable provisions of the Securities Exchange Act of 1934, and the rules and regulations thereunder, including, without limitation, Regulation M of the Securities Exchange Act of 1934, which may limit the timing of purchases and sales of any of the shares of common stock by the selling stockholder and any other participating person. Regulation M may also restrict the ability of any person engaged in the distribution of the shares of common stock to engage in market-making activities with respect to the shares of common stock. All of the foregoing may affect the marketability of the shares of common stock and the ability of any person or entity to engage in market-making activities with respect to the shares of common stock.

We will pay all expenses of the registration of the shares of common stock underlying the warrants held by the selling stockholder, including, without limitation, SEC filing fees and expenses of compliance with state securities or “blue sky” laws; provided, however, that the selling stockholder will pay all underwriting discounts and selling commissions, if any. We will indemnify the selling stockholder against liabilities, including liabilities under the Securities Act of 1933, in accordance with the investor rights agreement, or the selling stockholder will be entitled to contribution. We may be indemnified by the selling stockholder against civil liabilities, including liabilities under the Securities Act of 1933, that may arise from any written information furnished to us by the selling stockholder specifically for use in this prospectus, in accordance with the investor rights agreement, or we may be entitled to contribution.

Once sold under the registration statement of which this prospectus forms a part, the shares of common stock underlying the warrants held by the selling stockholder will be freely tradable by the purchasers of such shares, other than our affiliates.

Any shares covered by this prospectus that qualify for sale pursuant to Rule 144 of the Securities Act of 1933 may be sold under Rule 144, rather than pursuant to this prospectus.

DESCRIPTION OF CAPITAL STOCK

General

Our authorized capital stock consists of 100,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of undesignated preferred stock, \$0.0001 par value, of which no preferred shares are issued or outstanding.

The following summary description of our capital stock is based on the provisions of our certificate of incorporation and bylaws and the applicable provisions of the Delaware General Corporation Law. This information is qualified entirely by reference to the applicable provisions of our certificate of incorporation, bylaws and the Delaware General Corporation Law. For information on how to obtain copies of our certificate of incorporation and bylaws, please see “Where You Can Find Additional Information” and “Incorporation of Certain Information by Reference.”

Common Stock

As of March 15, 2017, there were 57,242,164 shares of our common stock outstanding. Holders of common stock will have voting rights for the election of our directors and all other matters requiring stockholder action, except with respect

Table of Contents

to amendments to our certificate of incorporation that alter or change the powers, preferences, rights or other terms of any outstanding preferred stock if the holders of such affected series of preferred stock are entitled to vote on such an amendment. There is no cumulative voting with respect to the election of directors, with the result that the holders of more than 50% of the shares voted for the election of directors can elect all of the directors. Holders of common stock will be entitled to one vote per share on matters to be voted on by stockholders and also will be entitled to receive such dividends, if any, as may be declared from time to time by our board of directors in its discretion out of funds legally available therefor. The payment of dividends, if ever, on the common stock will be subject to the prior payment of dividends on any outstanding preferred stock, of which there is currently none. Upon our liquidation or dissolution, the holders of common stock will be entitled to receive pro rata all assets remaining available for distribution to stockholders after payment of all liabilities and provision for the liquidation of any shares of preferred stock at the time outstanding. Our stockholders have no conversion, preemptive or other subscription rights and there are no sinking fund or redemption provisions applicable to the common stock.

Preferred Stock

Pursuant to our certificate of incorporation, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or stock exchange listing rules), to designate and issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the designations, powers, preferences, privileges and relative participating, optional or special rights and the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, voting rights, terms of redemption and liquidation preferences, any or all of which may be greater than the rights of the common stock, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

The board of directors, without stockholder approval, can issue preferred stock with voting, conversion or other rights that could adversely affect the voting power and other rights of the holders of common stock. Preferred stock could be issued quickly with terms designed to delay or prevent a change in control of our company or make removal of management more difficult. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of the common stock and may adversely affect the voting power of holders of common stock and reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation.

Our board of directors will fix the designations, voting powers, preferences and rights of the each series, as well as the qualifications, limitations or restrictions thereof, of the preferred stock of each series that we offer under this prospectus and applicable prospectus supplements in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. This description will include:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price per share;
- the dividend rate per share, dividend period and payment dates and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;

Table of Contents

- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock or other securities of ours, including depositary shares and warrants, and, if applicable, the conversion period, the conversion price, or how it will be calculated, and under what circumstances it may be adjusted;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange period, the exchange price, or how it will be calculated, and under what circumstances it may be adjusted;
- voting rights, if any, of the preferred stock;
- preemption rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material or special United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on issuances of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock being issued as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, rights, preferences, privileges, qualifications or restrictions of the preferred stock.

The General Corporation 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 (or, in some cases, as a series) on an amendment to our certificate of incorporation if the amendment would change the par value or, unless the certificate of incorporation provided otherwise, the number of authorized shares of the class or change the powers, preferences or special rights of the class or series so as to adversely affect the class or series, as the case may be. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Delaware Anti-Takeover Law and Provisions of our Certificate of Incorporation and Bylaws

Delaware Anti-Takeover Law.

As a Delaware corporation, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally has an anti-takeover effect for transactions not approved in advance by our board of directors. This may discourage takeover attempts that might result in payment of a premium over the market price for the shares of common stock held by stockholders. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a three-year period following the time that such stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A “business

Table of Contents

combination” includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An “interested stockholder” is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation’s voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; or
 - upon consummation of the transaction which 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 voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) shares owned by:
 - persons who are directors and also officers; and
 - employee stock plans, in some instances; or
- at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Staggered board of directors

Our Delaware certificate of incorporation provides that our board of directors will be classified into three classes of directors of approximately equal size at a date selected by the board. Currently our board of directors is not classified. As a result, in most circumstances, a person can gain control of our board only by successfully engaging in a proxy contest at two or more annual meetings.

Advance notice requirements for stockholder proposals and director nominations

Our Delaware bylaws provide that stockholders seeking to bring business before our annual meeting of stockholders, or to nominate candidates for election as directors at our annual meeting of stockholders, must provide timely notice of their intent in writing. To be timely, a stockholder’s notice needs to be delivered to our principal executive offices not later than the close of business on the 90th day nor earlier than the close of business on the 120th day prior to the first anniversary of the preceding year’s annual meeting of stockholders. Our bylaws also specify certain requirements as to the form and content of a stockholders’ meeting. These provisions may preclude our stockholders from bringing matters before our annual meeting of stockholders or from making nominations for directors at our annual meeting of stockholders.

Authorized but unissued shares

Our authorized but unissued shares of common stock and preferred stock are available for future issuances without stockholder approval and could be utilized for a variety of corporate purposes, including future offerings to raise additional capital, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved 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.

Table of Contents

Limitation on liability and indemnification of directors and officers

Our Delaware certificate of incorporation and bylaws provide that our directors and officers will be indemnified by us to the fullest extent authorized by Delaware law as it now exists or may in the future be amended, against all expenses and liabilities reasonably incurred in connection with their service for or on our behalf. Our bylaws permit us to secure insurance on behalf of any officer, director or employee for any liability arising out of his or her actions, regardless of whether Delaware law would permit indemnification.

These provisions may discourage stockholders from bringing a lawsuit against our directors for breach of their fiduciary duty. These provisions also may have the effect of reducing the likelihood of derivative litigation against directors and officers, even though such an action, if successful, might otherwise benefit us and our stockholders. Furthermore, a stockholder's investment may be adversely affected to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. We believe that these provisions, insurance and the indemnity agreements are necessary to attract and retain talented and experienced directors and officers.

Other than the two putative class action lawsuits in the United States District Court in the Central District of California, Napoli v. Ampio Pharmaceuticals, Inc., et al., Case No. 2:15 cv 03474 TJH and Stein v. Ampio Pharmaceuticals, Inc., et al., Case No. 2:15 cv 03640 TJH described in our Annual Report on Form 10 K and filed with the SEC on March 16, 2017, there is no pending litigation or proceeding involving any of our directors or officers where indemnification by us would be required or permitted, nor are we aware of any threatened litigation or proceeding that might result in a claim for such indemnification. Insofar as indemnification for liabilities arising under the Securities Act of 1933, or the Act, may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Corporate Stock Transfer, Inc., 3200 Cherry Creek Drive South, Suite 430, Denver, Colorado 80209.

Table of Contents

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any future debt securities we may offer under this prospectus, the applicable prospectus supplement or free writing prospectus will describe the specific terms of any debt securities offered through that prospectus supplement or free writing prospectus. The terms of any debt securities we offer under a prospectus supplement or free writing prospectus may differ from the terms we describe below. Unless the context requires otherwise, whenever we refer to the “indentures,” we are also referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue any senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue any subordinated debt securities under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. We have filed forms of these documents 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 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 indentures will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We use the term “trustee” to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplement or free writing prospectus and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete applicable indenture that contains the terms of the debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

We will describe in the applicable prospectus supplement or free writing prospectus the terms of the series of debt securities being offered, including:

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

Table of Contents

- 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, the conditions upon 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, if any at such time, to:
 - incur additional indebtedness;
 - issue additional securities;
 - create liens;
 - pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries;
 - 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; or
 - 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;
- 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;

Table of Contents

- 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 or advisable in connection with the marketing of the debt securities.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement or free writing prospectus 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 or free writing prospectus 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 other securities of ours 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 Indenture

Unless we provide otherwise in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, the following are events of default under the indentures with respect to any series of debt securities that we may issue:

- 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;
- 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 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 or free writing prospectus 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,

Table of Contents

may declare the unpaid 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.

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 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 or free writing prospectus.

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

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;
- to comply with the provisions described above under “—Consolidation, Merger or Sale;”

Table of Contents

- 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 Our 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 materially adversely affect the interests of any holder of debt securities of any series.

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 as otherwise provided in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, we and the trustee may make the following changes only 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 or free writing prospectus 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:

- 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;

Table of Contents

- 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.

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 or free writing prospectus, 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 or free writing prospectus with respect to that series.

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 or free writing prospectus, 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 or free writing prospectus, 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 or free writing prospectus 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. 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.

Table of Contents

Subject to this provision, the trustee 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.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, 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 or free writing prospectus, 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 or free writing prospectus, 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 or free writing prospectus 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.

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.

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 of Debt Securities

The subordinated debt securities will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement or free writing prospectus. 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 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.

Table of Contents

DESCRIPTION OF WARRANTS

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

We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant agreement, including a form of warrant certificate, that describes the terms of the particular series of warrants we are offering before the issuance of the related series of warrants. The following summaries of material provisions of the warrants and the 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 the particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplements related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete warrant agreements and warrant certificates that contain the terms of the warrants.

General

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

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- the number of shares of common stock purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
 - the manner in which the warrant agreements and warrants may be modified;
- a discussion of any material or special United States federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Table of Contents

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe 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.

Holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent.

Upon receipt of the required 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 issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate 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.

Governing Law

Unless we provide otherwise in the applicable prospectus supplement, the warrants and warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

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

DESCRIPTION OF UNITS

We may issue, in one or more series, units consisting of common stock and/or warrants for the purchase of common stock 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 units may be issued under unit agreements to be entered into between us and a unit agent, as detailed in the prospectus supplement relating to the units being offered. The prospectus supplement will describe:

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

- a description of the terms of any unit agreement governing the units;
- a description of the provisions for the payment, settlement, transfer or exchange of the units; and

Table of Contents

- whether the units if issued as a separate security will be issued in fully registered or global form.

While the terms summarized above will apply generally to any units that we may offer, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described above. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, any form of unit agreement, including any related agreements or certificates, that describes the terms of the particular series of units we are offering before the issuance of the related series of units. The material provisions of the units and any unit agreements are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and related agreements and certificates applicable to the particular series of units that we may offer under this prospectus. We urge you to read the applicable prospectus supplements related to the particular series of units that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete unit agreements and related agreements and certificates that contain the terms of the units.

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon by Goodwin Procter LLP, New York, New York. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements of Ampio Pharmaceuticals, Inc. as of December 31, 2016 and 2015 and for each of the years in the three-year period ended December 31, 2016, have been incorporated by reference herein from our Annual Report on Form 10-K for the year ended December 31, 2016, in reliance upon the report of EKS&H LLLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

This prospectus is part of a registration statement that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. We are a public company and file proxy statements, annual, quarterly and special reports and other information with the SEC. The registration statement, such reports and other information can be inspected and copied at the Public Reference Room of the SEC located at 100 F Street, N.E., Washington D.C. 20549. Copies of such materials, including copies of all or any portion of the registration statement, can be obtained from the Public Reference Room of the SEC at prescribed rates. You can call the SEC at 1-800-SEC-0330 to obtain information on the operation of the Public Reference Room. Such materials may also be accessed electronically by means of the SEC's home page on the Internet (www.sec.gov).

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 those documents instead of having to repeat the information in this prospectus. 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 that we have filed with the SEC:

- our Annual Report on Form 10-K for the year ended December 31, 2016, filed on March 16, 2017;
-

our Current Reports on Form 8-K filed on February 10, 2016, January 10, 2017, March 13, 2017 and March 28, 2017; and

Table of Contents

- the description of our common stock contained or incorporated by reference in our Registration Statement on Form 8-A, filed on May 17, 2011, including any amendment or reports filed for the purpose of updating this description.

We also incorporate by reference into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of the registration statement, or (ii) after the date of this prospectus until we sell all of the shares covered by this prospectus or the sale of shares by us pursuant to this prospectus is terminated.

You may access our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to any of these reports, free of charge on the SEC's website. You may also access the documents incorporated by reference on our website at www.ampiopharma.com. Other than the foregoing documents incorporated by reference, the information contained in, or that can be accessed through, our website is not part of this prospectus.

In addition, we will furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, on written or oral request of such person, a copy of any or all of the documents incorporated by reference in this prospectus (not including exhibits to such documents, unless such exhibits are specifically incorporated by reference in this prospectus or into such documents). Such requests may be directed to Ampio Pharmaceuticals, Inc., 373 Inverness Parkway, Suite 200, Englewood, Colorado 80112 or call (720) 437-6500.

Table of Contents

Up to \$24,650,000

Common Stock

Prospectus Supplement

Canaccord Genuity

April 12, 2019
