Ampio Pharmaceuticals, Inc.
Form 424B5
October 17, 2017

Filed pursuant to Rule 424(b)(5)
Registration No. 333-217094

PROSPECTUS SUPPLEMENT
(To Prospectus Dated April 20, 2017)

7,709,400 Shares Common Stock

We are offering 7,709,400 shares of our common stock, par value $0.0001 per share, in a registered direct offering at a negotiated price of $0.875 per share to certain investors that are not affiliated with us pursuant to this prospectus supplement and the accompanying prospectus and securities purchase agreements with such investors.

Our common stock is listed on the NYSE American under the symbol “AMPE.” The last reported sale price of our common stock on the NYSE American on October 13, 2017 was $1.08 per share. As of October 16, 2017, the aggregate market value of our common stock held by non-affiliates, or the public float, was $71,319,736, which was calculated based on 66,036,793 shares of our outstanding common stock held by non-affiliates as of the date of October 16, 2017 at a price of $1.08 per share, which was the closing price of our common stock on the NYSE American on October 13, 2017. As of the date hereof, we have sold an aggregate of approximately $23,725,653 of our securities, calculated 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.

Investing in our securities involves significant risks. Please read the information contained in or incorporated by reference under the heading “Risk Factors” beginning on page S-9 of this prospectus supplement, and under

similar headings in other documents filed after the date hereof and incorporated by reference into this prospectus supplement and the accompanying prospectus.

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

	Per Share	Total
Offering price	$ 0.875	$6,745,725
Placement agent fee(1)(2)	$ 0.046	$356,438
Proceeds, before expenses, to us	$ 0.829	$6,389,287

(1) We have engaged Joseph Gunnar & Co., LLC and Fordham Financial Management, Inc. to act as placement agents for this offering. We have agreed to reimburse the placement agents for certain of their expenses as described under the "Plan of Distribution" on page S-15 of this prospectus supplement.

(2) Represents a fee of 7% of the purchase price for the shares sold in the offering, excluding any purchase by an existing investor identified in the engagement agreement, on which the placement agents will not receive a fee, and including an advisory fee to be paid to the placement agents.

Delivery of the shares will take place on or about October 18, 2017, subject to the satisfaction of certain conditions.

Joseph Gunnar & Co. **Fordham Financial Management**

The date of this prospectus supplement is October 16, 2017.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of the registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a "shelf" registration process and consists of two parts. The first part is this prospectus supplement, which describes the specific terms of this offering. The second part, the accompanying prospectus, gives more general information, some of which may not apply to this offering. Generally, when we refer only to the "prospectus," we are referring to both parts combined. This prospectus supplement may add to, update or change information in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement or the accompanying prospectus.

If information in this prospectus supplement is inconsistent with the accompanying prospectus or with any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, you should rely on this prospectus supplement. This prospectus supplement, the accompanying prospectus and the documents incorporated into each by reference include important information about us, the securities being offered and other information you should know before investing in our securities. You should also read and consider information in the documents we have referred you to in the sections of this prospectus supplement entitled "Where You Can Find Additional Information" and "Incorporation of Certain Information by Reference."

You should rely only on this prospectus supplement, the accompanying prospectus, the documents incorporated or deemed to be incorporated by reference herein or therein and any free writing prospectus prepared by us or on our behalf. We have not authorized anyone to provide you with information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. If anyone provides you with different or inconsistent information, you should not rely on it. We are not offering to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus supplement, the accompanying prospectus or any free writing prospectus, or incorporated by reference herein, is accurate as of any date other than as of the date of this prospectus supplement or the accompanying prospectus or any free writing prospectus, as the case may be, or in the case of the documents incorporated by reference, the date of such documents regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our securities. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates.

All references in this prospectus supplement or the accompanying prospectus to "the Company," "our Company," "we," "us," or "our" mean Ampio Pharmaceuticals, Inc., unless we state otherwise or the context otherwise requires.

No action is being taken in any jurisdiction outside the United States to permit a public offering of the securities or possession or distribution of this prospectus supplement or the accompanying prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement or the accompanying prospectus

in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement or the accompanying prospectus applicable to that jurisdiction.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-3 (File No. 333-217094) under the Securities Act of 1933, as amended, or the Securities Act, with respect to the securities offered by this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus filed as part of the registration statement do not contain all the information set forth in the registration statement and its exhibits and schedules. For further information about us, we refer you to the registration statement and to its exhibits and schedules.

We file annual, quarterly and current reports and other information with the SEC. You may read and copy any materials we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information about the Public Reference Room. The SEC also maintains an internet website at www.sec.gov that contains periodic and current reports, proxy and information statements, and other information regarding registrants that file electronically with the SEC. Our common stock is listed on the NYSE American, and reports, proxy statements and other information concerning us can also be inspected at the offices of the NYSE, 20 Broad Street, New York, New York 10005.

These documents are also available, free of charge, through the investor relations section of our website, which is located at www.ampiopharma.com. Information contained on or accessible through our website is not incorporated by reference into this prospectus supplement or the accompanying prospectus and you should not consider information on or accessible through our website to be part of this prospectus supplement or the accompanying prospectus.

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 supplement and the accompanying prospectus. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and later information that we file with the SEC prior to the completion of this offering will automatically update and supersede this information. We incorporate by reference the documents listed below that we have filed with the SEC:

- description of our common stock contained in our Registration Statement on Form 8-A, filed on June 6, 2013;
- our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, filed on March 16, 2017;
- our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2017, filed on May 12, 2017, and the quarter ended June 30, 2017, filed on August 9, 2017;
- our Current Reports on Form 8-K filed on January 10, 2017, March 13, 2017, March 28, 2017, May 1, 2017, June 2, 2017, June 6, 2017, June 15, 2017, July 7, 2017, August 29, 2017, September 7, 2017, September 22, 2017, September 27, 2017 and October 16, 2017; and
- our definitive proxy statement on Schedule 14A filed on August 29, 2017.

We also incorporate by reference into this prospectus supplement and the accompanying 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 Securities Exchange Act of 1934, as amended, or the Exchange Act, after the date of this prospectus supplement until we sell all of the securities covered by this prospectus supplement and the accompanying prospectus or the sale of securities by us pursuant to this prospectus supplement and the accompanying prospectus is terminated.

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

You may request a copy of these documents, orally or in writing, which will be provided to you at no cost by contacting:

Ampio Pharmaceuticals, Inc.

373 Inverness Parkway, Suite 200,

Englewood, Colorado 80112

Attention: Chief Financial Officer

Telephone: (720) 437-6500

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein contain forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, 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,” “esti “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 expectations related to the use of proceeds, if any, from this offering;
- 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 (FDA), the European Medicines Agency (EMA), 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

- other factors discussed elsewhere in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein and therein.

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 supplement. 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 supplement, particularly in the section of this prospectus supplement 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 supplement after the date of this prospectus supplement except to the extent required by the federal securities laws. You should consider all risks and uncertainties disclosed in our filings with the SEC, described in the sections of this prospectus supplement entitled "Where You Can Find More Information" and "Incorporation of Certain Information by Reference" and the sections of the accompanying prospectuses entitled "Incorporation of Certain Information by Reference" and "Where You Can Find Additional Information," all of which are accessible on the SEC's website at www.sec.gov.

SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all the information that you should consider before investing in our securities. You should read the entire prospectus supplement and the accompanying prospectus carefully, including "Risk Factors" contained in this prospectus supplement and the financial statements incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision.

Company 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.

Background

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, Colorado, St. Anthony Hospital located in Lakewood, Colorado and the Medical Center of Plano, 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.

Business Overview

Our Product Pipeline

AMPION

Ampion for Osteoarthritis and Other Inflammatory Conditions

Ampion is the < 5 kDa ultrafiltrate of 5% Human Serum Albumin, or HSA, an approved biologic product. Ampion is a non-steroidal, low molecular weight, anti-inflammatory biologic, which has the potential to be used in a wide variety of acute and chronic inflammatory conditions, as well as immune-mediated diseases. We are currently developing Ampion as an intra-articular injection to treat pain due to severe osteoarthritis of the knee.

Ampion and its known components have demonstrated a broad spectrum of anti-inflammatory and immune modulatory activity which support the mechanism of action. We have published several scientific papers on Ampion, including three peer-reviewed publications, “The Low Molecular Weight Fraction of Commercial Human Serum Albumin (LMWF5A-Ampion) Induces Morphologic and Transcriptional Changes of Bone Marrow-Derived Mesenchymal Stem Cells”, “Anti-Inflammatory Activity in the Low Molecular Weight Fraction of Commercial Human Serum Albumin (LMWF5A)” and “Inflammatory pathways in knee osteoarthritis: potential targets for treatment”.

We have completed seven trials related to Ampion and recently completed enrollment and dosing of patients in a pivotal phase three trial for this product.

Clinical Development Pathway

In September and December 2016, we met with the Center for Biologics Evaluation and Research, or CBER, Division of the U.S. Food and Drug Administration, or FDA, to seek guidance on the best path forward to obtain a Biological License Application, or BLA, for Ampion to treat patients suffering from pain caused by severe osteoarthritis of the knee. As a result of these meetings, we continued our discussions with the FDA into the first quarter of fiscal 2017 while analyzing the best way to proceed towards filing our BLA for Ampion. Based on guidance from the FDA, we will conduct another Ampion trial that will be smaller than our prior trials with 168 patients, randomization of 6 to 1 (Ampion/Saline) on patients with severe osteoarthritis of the knee, defined radiologically as KL 4 patients. The 6-1 randomization will preserve blinding and prevent the bias in the assessment that might be associated with an unblinded evaluation; however, only Ampion treated patients will be evaluated. This 12-week study will evaluate the responder rate of Ampion treated patients as defined by Osteoarthritis Research Society International (“OARSI”), which includes pain, function, and patient global assessment (PGA). The outcome of this study will contribute to the label of Ampion which may include pain, function, and patient global assessment. Using the Outcome Measures in

Rheumatology Clinical Trials (“OMERACT”) OMERACT-OARSI responder rate definition and the analysis proposed in this protocol, all previous Ampion™ single injections clinical trials would have successfully met this endpoint. We believe this trial can be completed during the fourth quarter of fiscal 2017. If the trial is successful, we plan to file the BLA thereafter, pending any partnership discussions.

Future Development

We also intend to study Ampion for therapeutic applications outside of osteoarthritis of the knee and hand. We may engage development partners to study Ampion in various conditions including: (i) acute and chronic inflammatory conditions; (ii) degenerative joint diseases; and (iii) respiratory disorders. Based on the continuing evaluation, we are also studying Ampion's effects on cellular behavior to indicate potential effects on disease modification across multiple conditions. If successful, we believe these additional formulations and potential therapeutic indications will supplement the Ampion clinical portfolio, and will enable clinical applications in large therapeutic markets where there are significant unmet needs.

Market Opportunity

Osteoarthritis, or OA, is the most common form of arthritis, affecting over 100 million people in the United States with over 48 million people suffering from osteoarthritis of the knee. It is a progressive disorder of the joints involving degradation of the intra-articular cartilage, joint lining, ligaments, and bone. The incidence of developing osteoarthritis of the knee over a lifetime is approximately 45%. 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 subchondral bone. The global osteoarthritis of the knee market addresses moderate to moderately severe OA and is currently over $3.0 billion. We believe that this market does not account for the underserved severely diseased patients. The global demand for osteoarthritis of the knee treatment is expected to be fueled by aging demographics and increasing awareness of treatment options. Despite the size and growth of the osteoarthritis of the knee market, few adequate treatment options currently exist, especially in the severely diseased patient population.

Competition

The currently available treatments for osteoarthritis of the knee include oral non-steroidal anti-inflammatory agents, opioids, pain patches, intra-articular, or IA, corticosteroids, and IA hyaluronic acid, or HA, injections. Despite wide availability and years of clinical use, none of these agents are adequately meeting the needs of the market. In May 2013, the American Academy of Orthopedic Surgeons, or AAOS, issued their second edition of clinical practice guidelines for the treatment of osteoarthritis of the knee. The AAOS was unable to recommend for or against the use of intra-articular corticosteroid injections as studies designed to indicate efficacy are inconclusive. Further, the AAOS was also unable to recommend for or against the use of acetaminophen, opioids, or pain patches as the efficacy studies in this area are also inconclusive. Most importantly, the AAOS does not recommend (with a strong 'strength of recommendation') the use of hyaluronic acid injections as, in the AAOS' assessment, the clinical evidence does not support their use. This clinical practice guideline underscores a pervasive unmet need in the treatment of osteoarthritis

of the knee given few accepted and available treatments. We believe Ampion is a novel treatment option that, if approved, would be the first non-steroidal, non-hyaluronic-based intra-articular treatment available for the treatment of pain due to osteoarthritis of the knee.

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 an FDA compliant clean room to manufacture Ampion, research laboratories and our corporate offices.

We moved into our manufacturing facility in the summer of 2014. Since that time we have implemented a quality system, validated the facility for human-use products and produced Ampion. We presented on single use technology in manufacturing at the 24th Annual Aseptic Processing Technology Conference for the International Society for Pharmaceutical Engineers in February of 2015. We are now in the process of producing the FDA required registration batches of Ampion. The facility was placed in service during the first quarter of 2016. In our facility, we manufactured the Ampion drug and placebo (saline) for the PIVOT Trial and for the OA trial that we are currently conducting.

OPTINA

Optina for Diabetic Macular Edema

Optina is a low-dose formulation of danazol that we are developing to treat diabetic macular edema, or DME. Danazol is a synthetic derivative of modified testosterone ethisterone, and we believe it affects vascular endothelial cell linkage in a biphasic manner. At low doses, danazol decreases vascular permeability by increasing the barrier function of endothelial cells. The lipophilic low-molecular-weight weak androgen has the potential to treat multiple angiopathies. Steroid hormones control a variety of functions through slow genomic and rapid non-genomic mechanisms. Danazol immediately increases intracellular cyclic adenosine monophosphate through the rapid activation of membrane-associated androgen, steroid binding globulin, and calcium channel receptors. At lower concentrations, such as Optina, danazol binds to androgen and steroid binding globulin receptors stimulating the formation of a cortical actin ring. At higher concentrations, activation of the calcium channels shifts the balance towards stress fiber formation and increases vascular permeability.

When organized into a cortical ring, filamentous actin increases the barrier function of endothelial cells by tethering adhesion molecule complexes to the cytoskeleton. In this orientation, increased cortical actin improves tight junctions which strengthen cell-to-cell adhesions. Formation of the cortical actin ring thereby restricts leakage across the cell membrane.

We have completed two clinical trials of Optina and met with the Division of the Transplant and Ophthalmology Products of the FDA in late 2015 to discuss the results of the OptimEyes clinical trial of Optina and to seek guidance on the next steps to approval. The guidance from the FDA was that we perform a confirmatory study on patients with DME who are refractory to the currently available drugs, which if successful, would qualify Optina as a rescue medication for patients who have no treatment options (failed available therapies). The study could have significantly fewer patients than in our previous OptimEyes study, based on power calculations and guidance received from the FDA, and could include approximately 80 patients randomized 1:1 between placebo and Optina. Optina would be compared to placebo, not to other anti-VEGF drugs, since we are addressing a population that failed these alternative treatments. The FDA will consider improved vision as measured by best corrected visual acuity, which is statistically and clinically meaningful, as determined by experts in the field. The duration of the study is expected to be a maximum of 12 months. We have also considered conducting a trial in combination with other anti-VEGF drugs as we believe the effect of Optina with the anti-VEGF drugs could be cumulative.

The FDA has indicated that, for §505(b)(2) new drug applications, complete studies of the safety and effectiveness of a candidate product may not be necessary if appropriate bridging studies provide an adequate basis for reliance upon the FDA’s findings of safety and effectiveness for a previously approved product.

Corporate Information

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.

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 supplement.

THE OFFERING

The following is a brief summary of some of the terms of the offering and is qualified in its entirety by reference to the more detailed information appearing elsewhere in this prospectus supplement and the accompanying prospectus. For a more complete description of the terms of our common stock, see the "Description of Securities" section in this prospectus supplement and the "Description of Capital Stock" section in the accompanying prospectus.

Common stock we are offering	7,709,400 shares.
Common stock to be outstanding after this offering	75,941,809 shares.
NYSE American Symbol	Our common stock is quoted on the NYSE American under the symbol "AMPE."
Use of Proceeds	We estimate that the net proceeds from this offering, after payment of estimated offering expenses payable by us, will be approximately $6.3 million. We intend to use the net proceeds from this offering for working capital and general corporate purposes, including funding of the Ampion clinical trial. See "Use of Proceeds."
Risk Factors	Investing in our securities involves significant risks. Please read the information contained in or incorporated by reference under the heading "Risk Factors" beginning on page S-9 of this prospectus supplement, and under similar headings in other documents filed after the date hereof and incorporated by reference into this prospectus supplement and the accompanying prospectus.

The number of shares of common stock shown above to be outstanding after this offering is based on 68,232,409 shares outstanding as of June 30, 2017 and excludes:

- 7,797,498 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2017, at a weighted average exercise price of $3.36 per share;
- 2,427,503 shares of our common stock reserved for future issuance under our 2010 Stock Incentive Plan as of June 30, 2017; and
- 17,518,040 shares of our common stock issuable upon the exercise of warrants outstanding as of June 30, 2017, at a weighted average exercise price of $0.73 per share.

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RISK FACTORS

Investing in our securities involves a high degree of risk. In addition to the other information contained in this prospectus supplement and in the documents we incorporate by reference, you should carefully consider the risks discussed below and under the heading "Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 before making a decision about investing in our securities. The risks and uncertainties discussed below and in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 are not the only ones facing us. Additional risks and uncertainties not presently know to us may also harm our business. If any of these risks occur, our business, financial condition and operating results could be harmed, the trading price of our common stock could decline and you could lose part or all of your investment.

Risks Related to Our Common Stock and This Offering

Our stock price has been and could remain volatile, which could further adversely affect the market price of our stock, our ability to raise additional capital and/or cause us to be subject to securities class action litigation.

The market price of our common stock has historically experienced and may continue to experience significant volatility. In addition, in recent years, the stock market has experienced significant price and volume fluctuations. This volatility has affected the market prices of securities issued by many companies for reasons unrelated to their operating performance and may adversely affect the price of our common stock. Such market price volatility could adversely affect our ability to raise additional capital. In addition, we may be subject to securities class action litigation as a result of volatility in the price of our common stock, which could result in substantial costs and diversion of management's attention and resources and could harm our stock price, business, prospects, results of operations and financial condition.

The market price of our common stock may be adversely affected by market conditions affecting the stock markets in general, including price and trading fluctuations on the NYSE American.

Market conditions may result in volatility in the level of, and fluctuations in, market prices of stocks generally and, in turn, our common stock and sales of substantial amounts of our common stock in the market, in each case being unrelated or disproportionate to changes in our operating performance. Concerns over global stability and economic conditions in the United States and abroad have contributed to the extreme volatility of the markets which may have an effect on the market price of our common stock.

Future sales of common stock or warrants by existing stockholders could cause our stock price to decline and adversely impact the trading price of our common stock.

If our existing stockholders sell, or indicate an intent to sell, substantial amounts of our common stock or warrants in the public market, the trading price of our common stock could decline significantly and may be adversely impacted. We cannot predict the effect, if any, that future public sales of these securities or the availability of these securities for sale will have on the market and trading price of our securities. If our existing stockholders sell substantial amounts of our common stock or warrants in the public market, or if the public perceives that such sales could occur, this could have an adverse impact on the market and trading price of our securities, even if there is no relationship between such sales and the performance of our business.

In the future, we may sell additional shares of our common stock to raise capital or issue stock in connection with acquisitions. In addition, a substantial number of shares of our common stock are reserved for issuance upon the exercise of warrants, stock options and the vesting of restricted stock awards. We cannot predict the size of future issuances or the effect, if any, that they may have on the market price for our common stock. The issuance and sale of substantial amounts of common stock, or the perception that such issuances and sales may occur, could adversely affect the market price of our common stock or warrants and impair our ability to raise capital through the sale of additional equity securities.

You will experience immediate and substantial dilution in the net tangible book value per share of the common stock you purchase.

Since the offering price per share of the securities being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the offering price of $0.875 per share, if you purchase shares in this offering, you will suffer immediate and substantial dilution of $0.743 per share in the net tangible book value of the common stock. See the section entitled “Dilution” below for a more detailed discussion of the dilution you would incur if you purchase securities in this offering.

We may not be able to comply with the listing requirements of, and may be delisted from, the NYSE American.

In September 2017, we received a letter from the NYSE American, or the Exchange, stating that the Exchange had determined that we were not in compliance with Sections 1003(a)(ii) and 1003(a)(iii) of the Exchange Company Guide and the stockholders' equity continued listing standards applicable to us due to our recently reported stockholders' equity of $3,734,756 as of June 30, 2017 and net losses in our five most recent fiscal years ended December 31, 2016. We have submitted a plan advising the Exchange of the actions we have taken and will take to regain compliance with the continued listing standards by March 1, 2019. If our plan is accepted by the Exchange, then we will be able to continue our listing during the period ending March 1, 2019, during which time we will be subject to periodic reviews, including quarterly monitoring, for compliance with the plan. If the plan is not accepted, delisting proceedings will commence. Furthermore, if the plan is accepted by the Exchange, but we are not in compliance with the continued listing standards of the Exchange Company Guide by March 1, 2019, or if we do not make progress consistent with the plan, then the Exchange staff will initiate delisting proceedings as appropriate. We expect that following receipt of the proceeds from this offering we will be in compliance with the stockholders' equity continued listing standards applicable to us, however, there can be no assurances that we will be able to continue to comply with the Exchange listing requirements.

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion as to the use of the net proceeds from any offering by us and could use them for purposes other than those contemplated at the time of this offering. Accordingly, you will be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the proceeds will be invested in a way that does not yield a favorable, or any, return for our Company.

USE OF PROCEEDS

We estimate that the proceeds from this offering will be approximately $6.3 million, after deducting estimated offering expenses payable by us. We intend to use the net proceeds from this offering for working capital and general corporate purposes, including funding of the Ampion clinical trial. We have not determined the amounts we plan to spend on the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds from this offering. Pending application of the net proceeds as described above, we intend to invest the net proceeds of this offering in short-term, investment-grade, interest-bearing securities.

DILUTION

If you purchase shares of our common stock in this offering, you will experience dilution to the extent of the difference between the public offering price of the shares and the net tangible book value per share of our common stock immediately after this offering.

Our net tangible book value as of June 30, 2017 was approximately $3.7 million, or $0.055 per share of common stock. Net tangible book value per share is equal to our total tangible assets minus total liabilities, all divided by the number of shares of common stock outstanding as of June 30, 2017.

After giving effect to the sale of 7,709,400 shares of our common stock at a price of $0.875 per share, and after deducting offering expenses payable by us, our as adjusted net tangible book value would have been approximately $10.0 million, or approximately $0.132 per share of common stock, as of June 30, 2017. This represents an immediate increase in net tangible book value of approximately $0.077 per share to existing stockholders and an immediate dilution of approximately $0.743 per share to new investors. The following table illustrates this calculation on a per share basis:

Offering price per share		$0.875
Net tangible book value per share as of June 30, 2017	$0.055	
Increase in net tangible book value per share attributable to new investors	$0.077	
As adjusted net tangible book value per share after giving effect to this offering		$0.132
Dilution per share to investors in this offering		$0.743

The number of shares of common stock shown above to be outstanding after this offering is based on 68,232,409 shares outstanding as of June 30, 2017 and excludes:

- 7,797,498 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2017, at a weighted average exercise price of $3.36 per share;
- 2,427,503 shares of our common stock reserved for future issuance under our 2010 Stock Incentive Plan as of June 30, 2017; and
- 17,518,040 shares of our common stock issuable upon the exercise of warrants outstanding as of June 30, 2017, at a weighted average exercise price of $0.73 per share.

The above illustration of dilution per share to investors participating in this offering assumes no exercise of outstanding options to purchase our common stock or outstanding warrants to purchase shares of our common stock. The exercise of outstanding options and warrants having an exercise price less than the offering price will increase dilution to new investors. In addition, we may choose to raise additional capital depending on market conditions, our capital requirements and strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

PRICE RANGE OF COMMON STOCK

Our common stock is traded on the NYSE American. Prior to June 17, 2013, our common stock had been trading on the NASDAQ Capital Market under the ticker symbol “AMPE”, and prior to May 19, 2011, it was previously quoted on the Over-the-Counter Bulletin Board under the symbol “AMPE.OB.” The following table sets forth the intra-day high and low sale price information for our common stock as reported by the NYSE American, NASDAQ Capital Market and the Over-the-Counter Bulletin Board, for the respective periods that our common stock was traded thereon.

	High	**Low**
Year ending December 31, 2017		
1st Quarter	$1.05	$0.75
2nd Quarter	$1.04	$0.52
3rd Quarter	$0.78	$0.38
4th Quarter (through October 13, 2017)	$1.34	$0.61
Year ended December 31, 2016		
1st Quarter	$3.31	$1.90
2nd Quarter	$4.21	$1.29
3rd Quarter	$1.45	$0.70
4th Quarter	$1.14	$0.59
Year ended December 31, 2015		
1st Quarter	$7.60	$3.68
2nd Quarter	$7.38	$1.79
3rd Quarter	$3.12	$2.00
4th Quarter	$3.28	$2.51
Year ended December 31, 2014		
1st Quarter	$9.73	$5.70
2nd Quarter	$8.35	$5.44
3rd Quarter	$8.59	$3.33
4th Quarter	$4.16	$3.25

On October 13, 2017, the last reported sale price for our common stock on the NYSE American was $1.08 per share. As of October 16, 2017, there were of record approximately 270 holders of our common stock.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain our future earnings, if any, for use in our business and therefore do not anticipate paying cash dividends in the foreseeable future. Payment of future dividends, if any, will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs and plans for expansion.

PLAN OF DISTRIBUTION

We have entered into a securities purchase agreement with investors pursuant to which we will sell to such purchasers 7,709,400 shares of our common stock. The shares of our common stock will be sold to the investors in this offering at a negotiated price of $0.875 per share. We negotiated the prices of the securities offered in this offering with the investors. The factors considered in determining the price included the recent market price of our common stock, the general condition of the securities market at the time of this offering, the history of, and the prospects for, the industry in which we compete, our past and present operations, and our prospects for future revenues.

The securities purchase agreement contains customary representations, warranties and covenants for transactions of this type. We have also agreed to indemnify the investors against certain losses resulting from our breach of any of our representations, warranties, or covenants under agreements with the purchasers as well as under certain other circumstances described in the securities purchase agreement.

We will deliver the shares of common stock being issued to the investors electronically upon receipt of investor funds for the purchase of the shares of our common stock offered pursuant to this prospectus supplement. In the event an investor elects to make settlement through the placement agents, on the business day prior to the closing date of the offering, the Company will deliver to the placement agents electronically the shares purchased by such investor, and the placement agents will wire to the Company the net proceeds of such sale on the closing date. We currently anticipate that the closing of the sale of the shares of common stock offered pursuant to this prospectus supplement will take place, and we expect to deliver the shares of our common stock that are purchased, on or about October 18, 2017. The obligations of the investors to close this offering are subject to certain conditions, including the absence of any material adverse change in our business and the receipt of customary letters and certificates.

We estimate the total offering expenses of this offering that will be payable by us will be approximately $500,000, which include legal and printing costs and various other fees. At the closing, the Depository Trust Company will credit the common stock directly to investors at the address set forth in the securities purchase agreement.

In the securities purchase agreement, we have agreed, subject to certain exceptions, that we (or our subsidiaries) will not within 90 days following the closing of this offering, issue any equity securities or securities convertible into equity securities.

We have engaged Joseph & Gunnar & Co., LLC and Fordham Financial Management, Inc. to act as placement agents for the offering. We have agreed to pay the placement agents a fee of 7% of the aggregate purchase price for the securities sold in the offering, excluding any purchase by an existing investor identified in the engagement agreement,

on which the placement agents will not receive a fee. We have also agreed to reimburse the placement agents for certain expenses, including up to $2,500 for bound volumes and commemorative mementos, and up to $60,000 for fees and expenses of the placement agents' legal counsel. We have also agreed to pay Joseph Gunnar & Co., LLC an advisory fee of $115,763 upon the closing of the offering.

Our directors and officers have entered into lock-up agreements with Joseph Gunnar & Co., LLC. Under these agreements, these individuals have agreed, subject to specified exceptions, not to sell or transfer any common stock or securities convertible into, or exchangeable or exercisable for, our common stock during a period ending 90 days after the date of this prospectus supplement, without first obtaining the written consent of Joseph Gunnar & Co., LLC.

The placement agents for this offering also acted as the placement agents for our public offering that we completed in June 2017.

The foregoing description of the securities purchase agreement is only a summary, does not purport to be complete and is qualified in its entirety by reference to the securities purchase agreement, a copy of which is attached as an exhibit to our Current Report on Form 8-K filed with the SEC in connection with this offering and is incorporated herein by reference.

LEGAL MATTERS

The validity of the securities offered hereby has been passed upon for us by Goodwin Procter LLP, New York, New York. Sichenzia Ross Ference Kesner LLP, New York, New York, acted as counsel for the placement agents.

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.

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.

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.

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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."

1

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.

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;
- 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 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.

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,” “esti “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

- 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*.

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.

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.

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.

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					
	Shares of common stock beneficially owned prior to this offering(1) (2)		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)		
	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, Ugland House, South Church Street, George Town, Grand Cayman, KY 1-1104, Cayman Islands.

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.

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;
- 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 agents, any discounts, commissions and other terms constituting compensation from the selling stockholder and any discounts, commissions or concessions allowed or reallowed 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 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;
- 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 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.

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.

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;

- 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;

- 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, 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;"
- 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;
- 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.

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.

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.

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
- 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

- 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.

7,709,400 Shares of Common Stock

Joseph Gunnar & Co. Fordham Financial Management