Ampio Pharmaceuticals, Inc.
Form 424B5
February 10, 2016
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Registration No. 333-193096

PROSPECTUS SUPPLEMENT

(to Prospectus dated January 22, 2014)

AMPIO PHARMACEUTICALS, INC.

Up to $25,000,000

Common Stock

We have entered into a Controlled Equity Offering℠ Sales Agreement, or the Sales Agreement, with Cantor Fitzgerald & Co., or Cantor Fitzgerald, relating to shares of our common stock, par value $0.0001 per share, offered by this prospectus supplement. In accordance with the terms of the Sales Agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to $25,000,000 from time to time through Cantor Fitzgerald, acting as sales agent. Sales of the shares of common stock, if any, may be made on the NYSE MKT LLC, or the NYSE MKT, at market prices and such other sales as agreed upon by us and Cantor Fitzgerald.

Our common stock is listed on the NYSE MKT under the symbol AMPE. On February 8, 2016, the last reported sale price of our common stock on the NYSE MKT was $2.08 per share.

Sales of our common stock, if any, under this prospectus supplement may be made in sales deemed to be at-the-market equity offerings as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through the NYSE MKT, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or any other method permitted by law. Cantor Fitzgerald will act as sales agent on a best efforts basis and use commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with its normal trading and sales practices, on mutually agreed terms between Cantor Fitzgerald and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Cantor Fitzgerald will be entitled to compensation at a fixed commission rate of 3.0% of the gross sales price per share sold. In connection with the sale of our common stock on our behalf, Cantor Fitzgerald will be deemed to be an underwriter within the meaning of the Securities Act and the compensation of Cantor Fitzgerald will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cantor Fitzgerald with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Investing in our securities involves a high degree of risk. See Risk Factors beginning on page S-7 of this prospectus supplement and in the other documents that are incorporated by reference in 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.

The date of this prospectus supplement is February 10, 2016.

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PROSPECTUS SUPPLEMENT

PROSPECTUS

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering and supplements information contained in the accompanying prospectus and the documents incorporated by reference into the accompanying prospectus. The second part is the accompanying prospectus filed with the Securities and Exchange Commission, or the SEC, as part of a registration statement on Form S-3 (File No. 333-193096) that became effective on January 22, 2014. The second part gives more general information about us and the shares of common stock we may offer from time to time pursuant to the registration statement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or any document incorporated by reference therein, on the other hand, the information in this prospectus supplement shall control.

You should read this prospectus supplement, the accompanying prospectus, the documents and information incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering when making your investment decision. You should also read and consider the information in the documents we have referred you to under the headings Where You Can Find More Information and Incorporation of Certain Information by Reference.

You should rely only on the information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus. We have not, and the sales agent has not, authorized anyone to provide you with information that is different. We are offering to sell and seeking offers to buy shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus supplement, the accompanying prospectus, the documents and information incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering are accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement or of any sale of our common stock.

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

Unless otherwise mentioned or unless the context requires otherwise, throughout this prospectus supplement and any related free writing prospectus, the words Ampio Pharmaceuticals, Ampio, we, us, our, the company or similar references refer to Ampio Pharmaceuticals, Inc. and its subsidiaries on a consolidated basis. References to BioSciences in this prospectus supplement mean DMI BioSciences, Inc., now a wholly-owned subsidiary of ours. References to Life Sciences in this prospectus supplement mean DMI Life Sciences, Inc., which is our predecessor for accounting purposes and a wholly-owned subsidiary of ours. Life Sciences was formed in December 2008 and commenced operations when it acquired certain assets of BioSciences in April 2009. In March 2010, Life Sciences merged with a subsidiary of Chay Enterprises, Inc., a publicly traded Colorado corporation, which we refer to in this prospectus supplement as Chay Enterprises. Immediately after the merger, Chay Enterprises changed its name to Ampio Pharmaceuticals, Inc., and reincorporated in Delaware. We acquired BioSciences, now a wholly-owned subsidiary of ours, in March 2011.

This prospectus supplement and the information incorporated herein by reference includes trademarks, such as Ampion and Optina, which are protected under applicable intellectual property laws and are our property or the property of our subsidiaries. This prospectus supplement may also contain trademarks, service marks, copyrights and trade names of other companies which are the property of their respective owners. Solely for convenience, our trademarks and tradenames referred to in this prospectus supplement may appear without the ® or symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights to these trademarks and tradenames.

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

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information about us and this offering and does not contain all of the information that you should consider in making your investment decision. You should carefully read this entire prospectus supplement and the accompanying prospectus, including the risks and uncertainties discussed under the heading Risk Factors beginning on page S-7 of this prospectus supplement, and the information incorporated by reference in this prospectus supplement and the accompanying prospectus, including our consolidated financial statements, before making an investment decision. If you invest in our securities, you are assuming a high degree of risk.

Company Overview

Ampio Pharmaceuticals, Inc. is a biopharmaceutical company focused primarily on the development of therapies to treat prevalent inflammatory conditions for which there are limited treatment options. Our two lead product candidates in development are Ampion for osteoarthritis of the knee and Optina for diabetic macular edema.

Background

Our product portfolio is primarily based on the work of Dr. David Bar-Or, the Director of Trauma Research LLC for both the Swedish Medical Center located in Englewood, Colorado and St. Anthony Hospital located in Lakewood, Colorado. For over two decades, while directing these two trauma research laboratories, Dr. Bar-Or and his staff have built a robust portfolio of product candidates focusing on inflammatory conditions. Ampio s 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 a sub 5,000 molecular weight fraction of commercial human serum albumin, or HSA. The primary constituent ingredient is aspartyl-alanyl diketopiperazine, or DA-DKP, an endogenous immunomodulatory molecule derived from the N-terminus of HSA. Based on our published in-vitro findings, DA-DKP appears to play a significant role in the homeostasis of inflammation. DA-DKP is believed to reduce inflammation by suppressing pro-inflammatory cytokine production in T-cells. Ampion also contains other known small molecules that confer anti-inflammatory effects to complement the activity of DA-DKP and derive in-vitro and in-vivo effects. We believe the non-steroidal, low molecular weight, anti-inflammatory biologic 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 osteoarthritis of the knee.

Ampion is manufactured as the low molecular weight filtration product of commercial human serum albumin containing DA-DKP, N-acetyltryptophan, caprylate, and other small molecules either contained in HSA or added to HSA during the processing and production of commercial HSA products. DA-DKP, the primary constituent ingredient contained in Ampion, is a locally generated molecule formed as a physiological result of the cleavage and cyclization of the N-terminal aspartic acid and alanine residues of human albumin. The molecule was originally discovered in the blood and cerebrospinal fluid of patients several days after suffering severe closed head

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injuries. A high concentration of DA-DKP has also been detected in biofilms found on endotracheal tubes recovered from intubated patients and on implanted orthopedic plates and screws. Together these findings suggest a mechanism by which DA-DKP contributes to the ability to reduce the body s inflammatory response following insult or injury.

DA-DKP is believed to reduce inflammation through the activation of Ras-related protein 1, or Rap1. Rap1 interrupts the kinase cascade by regulating the amount of rapidly accelerated fibrosarcoma, or Raf, kinases available for interaction with Ras, inhibiting antigen-specific Ras activation. This decrease disrupts the mitogen-activation protein kinase, or MAPK, cascade and results in decreased immunoinflammatory cytokine gene transcription. The clinical results which are detailed below also suggest an effect other than anti-inflammatory properties are at work and imply more prolonged healing-like effects.

We have published several scientific papers on Ampion. Most recently in June 2015 we announced 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 and 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 .

Market Opportunity

Osteoarthritis 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 continues to expand and is currently over $3.0 billion. 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. We believe that if Ampion proves to be effective in the most severe patients, the market could grow substantially.

Ampion Clinical Development

We have completed multiple clinical trials in the development of Ampion. Clinical trial development began in 2011 with a Phase I/II study. In 2013, we announced the results of the single injection Phase III SPRING study, which met its primary endpoint, and was deemed by the U.S. Food and Drug Administration, or the FDA, as one of the two pivotal trials required to support a Biologics License Application, or BLA. Results of the SPRING study have been published. Multiple injections were evaluated in the first and second quarter of 2015. The multiple injection Phase II STRUT study demonstrated a 64% reduction in pain over baseline at 20 weeks. The multiple injection STRIDE study did not reach its primary endpoint, though it did demonstrate a significant reduction in pain over baseline at 20 weeks. In July 2015, we held an investor call and announced our meeting with the FDA where a single injection clinical trial and a Special Protocol Assessment, or SPA, were recommended by the FDA as the second, and final, pivotal trial for the BLA. An SPA is a process by which the FDA provides written agreement on the design and size of a clinical protocol for the purpose of BLA filing. An SPA can significantly de-risk the path to market due to insufficient data or unexpected safety concerns. In September 2015, we announced the FDA awarded us an SPA and the second Phase III pivotal trial of Ampion had begun. The clinical trial is currently underway.

Competition

The currently available treatments for osteoarthritis of the knee include oral non-steroidal anti-inflammatory agents, opioids, pain patches, intra-articular corticosteroids, and IA hyaluronic acid 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

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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, and in the association s assessment, the clinical evidence does not support their use. This latest 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 osteoarthritis of the knee.

Ampion Manufacturing Facility

We moved into our new 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 the product used in the PIVOT study clinical trial. 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 2015. We are now in the final stages of the FDA required registration batches and have begun to manufacture inventory that could potentially be used commercially. We believe that these steps will shorten our regulatory timelines and significantly reduce our time to commercial market.

Future Development

We intend to study Ampion for therapeutic applications outside of osteoarthritis of the knee. We are investigating the possible use of Ampion for pain due to osteoarthritis of the hand and as a potential relief for ocular conditions. 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.

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 shift the balance towards stress fiber formation and increase 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.

Market Opportunity

Type 1 and Type 2 diabetes mellitus affects 26 million people in the United States. One of the many symptoms of diabetes is the local and systemic inflammation of the microvascular system. Diabetic retinopathy is a complication of diabetes and is characterized by damage to the blood vessels of the retina and can either be proliferative or non-proliferative. Proliferative damage occurs when a reduction in oxygen levels in the retina due to impaired glucose metabolism causes fragile blood vessels to grow in the vitreous humor. Non-proliferative damage occurs when existing vessels experience poor endothelial cell linkage due to increased blood glucose levels and hypertension. Macular edema is the most common form of non-proliferative diabetic retinopathy. In diabetic macular edema, prolonged hyperglycemia compromises endothelial cell linkage leading to vascular permeability.

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The leakage of fluid, solutes, proteins and immune cells cause the macula to swell and thicken. This leads to damage of the central retinal tissue and can significantly impair sharp central vision. The prevalence of diabetes is 11.3% of the population above the age of 20, with an annual incidence of 1.9 million cases in the United States alone. In this population, the prevalence of diabetic macular edema is estimated at 30% of patients inflicted by the disease for 20 years or more.

Competition

There are no orally administered treatments for DME currently available nor to our knowledge are any being tested in clinical trials. The current standard of care in the U.S. for the treatment of DME is laser photocoagulation. The first and only approved therapy in the U.S. is intravitreal ranibizumab-injections. Ranibizumab belongs to a therapeutic class inhibiting vascular endothelial growth factor, or anti-VEGF. It is important to note, there is significant competition from off-label anti-VEGF treatment of DME from bevacizumab. Iluvien, a fluocinolone acetonide micro-insert intravitreous implant, is available in six European countries, and is pending approval in the United States while its sponsor reportedly resolves manufacturing issues. Dexamethasone intravitreal implant is available in the U.S. for macular edema following retinal vein occlusion and noninfectious uveitis and the product s sponsor has submitted for U.S. and European approval in the treatment of DME. Aflibercept, another anti-VEGF antibody treatment, is also awaiting U.S. and European approval in the treatment of DME.

Optina Clinical Development

In 2012, we announced results for a Phase II study. In November 2014, we announced the completion of the OptimEyes study and the beginning of statistical analysis. In May 2015, we announced initial results for the OptimEyes study and released additional analysis in July 2015, which showed Optina is effective when given at the correct dose for body mass index in a subset of patients. Additionally, analysis demonstrated a synergistic effect of Optina with common kidney-induced high blood pressure medications (angiotensin receptor blocker and angiotensin converting enzyme inhibitor). In October 2015, following a meeting with the FDA, we announced updates on the regulatory path for FDA approval of Optina. 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 will have approximately 80 patients randomized 1:1 between placebo and Optina, which is significantly fewer patients than in the previous OptimEyes study; Optina will be compared to placebo, not to anti-vascular endothelial growth factor drugs; the FDA will consider improved vision as measured by Best Corrected Visual Acuity, which is statistically significant and clinically meaningful as determined by experts in the field; the duration of the study will be a maximum of 12 months.

NCE 001

Para-phenoxy-methylphenidate is a novel, small molecule methylphenidate derivative. Its basic mechanism of action is believed to be to increase methylation of the catalytic sub-unit of Protein Phosphatase 2 A, or PP2A, with activation of this phosphatase achieving an effect similar to kinase inhibitors. PP2A is known to be largely involved in inflammation, angiogenesis, and cell proliferation, and by decreasing phosphorylation, the intracellular phosphatase inhibits pro-carcinogenic cytokines and chemokines and cell signaling factors. Our pre-clinical research is focused on neuroblastoma, glioblastoma multiforme, renal cell carcinoma, and inflammatory breast cancer.

Corporate Update

On January 28, 2016, we held a conference call during which we announced that our cash and cash equivalents on a consolidated basis at December 31, 2015 was $27.0 million. We also announced that our cash and cash equivalents on a standalone basis at December 31, 2015 was $16.0 million, excluding any cash and cash equivalents held at Aytu BioScience, Inc., or Aytu, an entity that we owned 81.5% of as of that same date. On January 4, 2016, we completed a distribution of 10,399,661 Aytu shares to our shareholders, reducing our ownership in Aytu to below 10% on January 5, 2016.

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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.

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THE OFFERING

Common stock offered by us pursuant to this prospectus supplement	Shares of our common stock having an aggregate offering price of up to $25,000,000.
Common stock to be outstanding after this offering	Up to 64,017,536 shares (as more fully described in the notes following this table), assuming sales of 12,019,230 shares of our common stock in this offering at an offering price of $2.08 per share, which was the last reported sale price of our common stock on the NYSE MKT on February 8, 2016. The actual number of shares issued will vary depending on the sales price under this offering.
Manner of offering	At-the-market offering that may be made from time to time through our sales agent, Cantor Fitzgerald. See Plan of Distribution on page S-14 of this prospectus supplement.
Use of Proceeds	We currently intend to use the net proceeds primarily for general corporate purposes. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses of the proceeds. As a result, our management will retain broad discretion in the allocation and use of the net proceeds. See Use of Proceeds on page S-11 of this prospectus supplement.
Risk Factors	An investment in our common stock involves a high degree of risk. See the information contained in or incorporated by reference under Risk Factors on page S-7 of this prospectus supplement, page 19 of our Annual Report on Form 10-K for the year ended December 31, 2014 and under similar headings in the other documents that are incorporated by reference herein, as well as the other information included in or incorporated by reference in this prospectus supplement.
NYSE MKT symbol	AMPE

The number of shares of our common stock to be outstanding after this offering is based on 51,998,306 shares of common stock outstanding as of September 30, 2015. Unless specifically stated otherwise, the information in this prospectus supplement is as of September 30, 2015 and excludes:

- 7,155,832 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2015, at a weighted average exercise price of $3.72 per share, of which options to purchase 5,985,940 shares of our common stock were then exercisable;

- 499,076 shares of our common stock issuable upon the exercise of warrants at a weighted average exercise price of $3.24 per share; and

an aggregate of 3,149,773 shares of our common stock reserved for future grants of stock options under our 2010 Stock Incentive Plan.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should carefully consider the risks described below, together with all of the other information contained in this prospectus supplement, and accompanying prospectus and incorporated by reference herein and therein, including from our most recent Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q. Some of these factors relate principally to our business and the industry in which we operate. Other factors relate principally to your investment in our securities. The risks and uncertainties described below are not the only risks facing us. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also materially and adversely affect our business and operations. Subsequent to the quarterly period covered by our Quarterly Report on Form 10-Q for the three months ended September 30, 2015, there were no material changes to the risk factors, except as updated below.

If any of the matters included in the following risks were to occur, our business, financial condition, results of operations, cash flows or prospects could be materially and adversely affected. In such case, you may lose all or part of your investment.

Risks Related to our Business

If we do not receive marketing approval for Ampion, we may not realize the investment we have made in our manufacturing facility.

In December 2013, we entered into a ten-year lease of a multi-purpose facility containing approximately 19,000 square feet. We have spent approximately $10.4 million to build out this facility in anticipation of receiving approval of our BLA and commencing commercialization of Ampion. If the FDA does not approve our BLA for Ampion, or does not approve of our manufacturing operation, we will not be able to manufacture and commercialize Ampion in our new facility and we will remain obligated to make payments under our lease, which is set to expire in 2023. Any delay or failure to receive BLA approval for Ampion could have a material adverse effect on our financial condition and results of operations.

Risks Related to this Offering

You will experience immediate and substantial dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 12,019,230 shares of our common stock are sold at a price of $2.08 per share, the last reported sale price of our common stock on the NYSE MKT on February 8, 2016, for aggregate gross proceeds of $25.0 million, and after deducting commissions and estimated offering expenses payable by us, you will experience immediate dilution of $1.13 per share, representing the difference between our as adjusted net tangible book value per share as of September 30, 2015 after giving effect to this offering and the assumed offering price. The exercise of outstanding stock options and warrants will result in further dilution of your investment. See the section entitled Dilution below for a more detailed illustration of the dilution you would incur if you participate in this offering.

A substantial number of shares may be sold in the market following this offering, which may depress the market price for our common stock.

Sales of a substantial number of shares of our common stock in the public market following this offering could cause the market price of our common stock to decline. Although there can be no assurance that all $25.0 million worth of shares being offered under this prospectus supplement will be sold or the price at which any such shares might be sold, assuming that an aggregate of 12,019,230 shares of our common stock are sold during the term of the Sales Agreement with Cantor Fitzgerald, in each case, for example, at a price of $2.08 per share, the last reported sale price of our common stock on the NYSE MKT on February 8, 2016, upon completion of this offering, based on our shares outstanding as of September 30, 2015, we will have outstanding an aggregate of 64,017,536 shares of common stock, assuming no exercise of outstanding stock options or convertible promissory notes. A substantial majority of the outstanding shares of our common stock are, and all of the shares sold in this offering upon issuance will be, freely tradable without restriction or further registration under the Securities Act, unless these shares are owned or purchased by affiliates as that term is defined in Rule 144 under the Securities Act.

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You may experience future dilution as a result of future equity offerings or other equity issuances.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to the rights of existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

We have broad discretion in the use of the net proceeds of this offering and, despite our efforts, we may use the net proceeds in a manner that does not increase the value of your investment.

We currently intend to use the net proceeds from this offering for the general corporate purposes, which may include continued research and development, expenses related to Ampion, Optina and other product candidates, capital expenditures, working capital and general and administrative expenses. However, we have not determined the specific allocation of the net proceeds among these potential uses. Our management will have broad discretion over the use and investment of the net proceeds of this offering, and, accordingly, investors in this offering will need to rely upon the judgment of our management with respect to the use of proceeds, with only limited information concerning our specific intentions. These proceeds could be applied in ways that do not improve our operating results or increase the value of your investment. Please see the section entitled Use of Proceeds on page S-11 of this prospectus supplement for further information.

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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 of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Forward-looking statements are those that predict or describe future events or trends and that do not relate solely to historical matters. You can generally identify forward-looking statements as statements containing the words believe, expect, may, will, anticipate, intend, estimate, project, plan, assume or other similar expr 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

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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 Securities and Exchange Commission, or 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.

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USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to $25.0 million from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize the Sales Agreement with Cantor Fitzgerald as a source of financing.

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. Except as described in 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 hereby for general corporate purposes, which may include continued research and development, expenses related to Ampion, Optina and other product candidates, capital expenditures, working capital and general and administrative expenses. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to our own, although we have no commitments or agreements with respect to any acquisitions as of the date of this prospectus supplement. Pending these uses, we intend to invest the net proceeds primarily in government securities and short-term, interest-bearing securities.

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DILUTION

Our net tangible book value as of September 30, 2015 was approximately $36.8 million, or $0.71 per share of common stock. Net tangible book value per share is determined by dividing total tangible assets less total liabilities, excluding items such as intangibles and non-cash GAAP adjustments, by the aggregate number of shares of common stock outstanding as of September 30, 2015. Dilution per share to new investors represents the difference between the amount per share paid by purchasers for our common stock in this offering and the net tangible book value per share of our common stock immediately following the completion of this offering.

After giving effect to the sale of shares of common stock offered by the prospectus at an assumed public offering price of $2.08 per share of common stock (the last reported sale price of our common stock on NYSE MKT on February 8, 2016), and after deducting the commissions and estimated aggregate offering expenses payable by us, our net tangible book value as of September 30, 2015 would have been approximately $60.9 million, or $0.95 per share of common stock. This represents an immediate increase in net tangible book value of $0.24 per share to our existing stockholders and an immediate dilution of $1.13 per share of common stock issued to the new investors purchasing securities in this offering.

The following table illustrates this per share dilution:

Assumed public offering price per share of common stock		$ 2.08
Net tangible book value per share as of September 30, 2015	$ 0.71	
Increase per share attributable to new investors	$ 0.24	
Net tangible book value per share after this offering		$ 0.95
Dilution per share to new investors		$ 1.13

The table above assumes for illustrative purposes that an aggregate of 12,019,230 shares of our common stock are sold at a price of $2.08 per share, the last reported sale price of our common stock on the NYSE MKT on February 8, 2016, for aggregate gross proceeds of approximately $25,000,000. The shares sold in this offering, if any, will be sold from time to time at various prices. An increase of $1.00 per share in the price at which the shares are sold from the assumed offering price of $2.08 per share shown in the table above, assuming all of our common stock in the aggregate amount of $25,000,000 is sold at that price, would increase our adjusted net tangible book value per share after the offering to $1.01 per share and would increase the dilution in net tangible book value per share to new investors to $2.07 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of $1.00 per share in the price at which the shares are sold from the assumed offering price of $2.08 per share shown in the table above, assuming all of our common stock in the aggregate amount of $25,000,000 is sold at that price, would increase our net tangible book value per share after the offering to $0.81 per share and would decrease the dilution in net tangible book value per share to new investors to $0.27 per share, after deducting commissions and estimated aggregate offering expenses payable by us.

The information discussed above is illustrative only and will adjust based on the actual public offering price and other terms of this offering determined at pricing.

The above table is based on 51,998,306 shares of common stock outstanding as of September 30, 2015. Unless specifically stated otherwise, the information in this prospectus supplement is as of September 30, 2015 and excludes:

7,155,832 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2015, at a weighted average exercise price of $3.72 per share, of which options to purchase 5,985,940 shares of our common stock were then exercisable;

499,076 shares of our common stock issuable upon the exercise of warrants at a weighted average exercise price of $3.24 per share; and

an aggregate of 3,149,773 shares of our common stock reserved for future grants of stock options under our 2010 Stock Incentive Plan.

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To the extent that options or warrants are exercised, new options are issued under 2010 Stock Incentive Plan, or we issue additional shares of common stock in the future, there may be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If 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.

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PLAN OF DISTRIBUTION

We have entered into a Controlled Equity Offering[SM] Sales Agreement, dated February 10, 2016, or the Sales Agreement, with Cantor Fitzgerald, under which we may offer and sell shares of our common stock having an aggregate gross sales price of up to $25,000,000 from time to time through Cantor Fitzgerald acting as agent. Sales of the shares of common stock, if any, may be made on the NYSE MKT at market prices and such other sales as agreed upon by us and Cantor Fitzgerald. The Sales Agreement has been filed as an exhibit to a Current Report on Form 8-K under the Exchange Act and incorporated by reference into this prospectus supplement.

Upon delivery of a placement notice and subject to the terms and conditions of the Sales Agreement, Cantor Fitzgerald may sell our common stock by any method permitted by law deemed to be an at-the-market offering as defined in Rule 415 promulgated under the Securities Act, including sales made directly on the NYSE MKT, on any other existing trading market for our common stock or to or through a market maker. Cantor Fitzgerald may also sell our common stock by any other method permitted by law, including in privately negotiated transactions with our prior written consent. We may instruct Cantor Fitzgerald not to sell common stock if the sales cannot be effected at or above the price designated by us from time to time.

We will pay Cantor Fitzgerald commissions, in cash, for its services in acting as agent in the sale of our common stock. Cantor Fitzgerald will be entitled to compensation at a commission rate of 3.0% of the aggregate gross proceeds from each sale of our common stock. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. If so requested by Cantor Fitzgerald, and unless otherwise agreed, we will reimburse Cantor Fitzgerald for certain specified expenses, including the fees and disbursements of its legal counsel, in an amount not to exceed $50,000. We estimate that the total expenses for the offering, excluding compensation and reimbursements payable to Cantor Fitzgerald under the terms of the Sales Agreement, will be approximately $50,000.

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

Cantor Fitzgerald will use its commercially reasonable efforts, consistent with its normal sales and trading practices and applicable state and federal laws, rules and regulations and the rules of the NYSE MKT, to solicit offers to purchase the common stock shares under the terms and subject to the conditions set forth in the Sales Agreement. In connection with the sale of the common stock on our behalf, Cantor Fitzgerald will be deemed to be an underwriter within the meaning of the Securities Act and the compensation of Cantor Fitzgerald will be deemed to be underwriting commissions or discounts. We or Cantor Fitzgerald may suspend the offering of shares of common stock by notifying the other. We have agreed to provide indemnification and contribution to Cantor Fitzgerald against certain civil liabilities, including liabilities under the Securities Act.

The offering of our common stock pursuant to the Sales Agreement will terminate upon the earlier of (1) the sale of all shares of our common stock subject to the Sales Agreement or (2) termination of the Sales Agreement as permitted therein. We and Cantor Fitzgerald may each terminate the Sales Agreement at any time upon 10 days prior notice.

Cantor Fitzgerald and its affiliates may in the future provide various investment banking, commercial banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To

the extent required by Regulation M, Cantor Fitzgerald will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus supplement.

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

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LEGAL MATTERS

The validity of the securities we are offering will be passed upon by Goodwin Procter LLP, New York, New York. Cantor Fitzgerald is being represented in connection with this offering by Cooley LLP, New York, New York.

EXPERTS

The consolidated financial statements of Ampio Pharmaceuticals, Inc. appearing in Ampio Pharmaceuticals Inc. s Annual Report on Form 10-K for the year ended December 31, 2014, and the effectiveness of Ampio Pharmaceutical, Inc. s internal control over financial reporting as of December 31, 2014, have been audited by EKS&H LLLP, an independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act, of which this prospectus supplement and the accompanying prospectus form a part. The rules and regulations of the SEC allow us to omit from this prospectus supplement certain information included in the registration statement. For further information about us and the securities we are offering under this prospectus supplement, you should refer to the registration statement and the exhibits and schedules filed with the registration statement. With respect to the statements contained in this prospectus supplement regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement.

Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC s website at *www.sec.gov*. You may also read and copy any document 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 on the operation of the Public Reference Room.

We make available free of charge on our website our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the SEC. Please note, however, that we have not incorporated any other information by reference from our website, other than the documents listed under the heading Incorporation of Certain Information by Reference on page S-16 of this prospectus supplement. In addition, you may request copies of these filings at no cost by writing or telephoning us at the following address or telephone number:

Ampio Pharmaceuticals, Inc.

373 Inverness Parkway, Suite 200,

Englewood, Colorado 80112

Attention: Chief Financial Officer

Telephone: (720) 437-6500

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INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information into this prospectus supplement. This means that we can disclose important information to you by referring you to other documents we have filed separately with the SEC, without actually including the specific information in this prospectus supplement. The information incorporated by reference is considered to be part of this prospectus supplement, and information that we file later with the SEC (and that is deemed to be filed with the SEC) will automatically update, and may supersede, information in this prospectus supplement.

This prospectus supplement incorporates by reference the documents set forth below that have previously been filed with the SEC:

- Our Annual Report on Form 10-K for the year ended December 31, 2014 filed with the SEC on February 24, 2015;
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2015 filed with the SEC on May 8, 2015;
- Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2015 filed with the SEC on August 7, 2015;
- Our Quarterly Report on Form 10-Q for the quarter ended September 30, 2015 filed with the SEC on November 6, 2015;
- Our Definitive Proxy Statement on Schedule 14A filed with the SEC on November 12, 2015, to the extent incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2014;
- Our Current Reports on Form 8-K filed with the SEC on April 21, 2015 (except Item 7.01 and Exhibit 99.1), April 22, 2015, May 26, 2015 (except Item 7.01 and Exhibit 99.1), May 27, 2015, August 6, 2015, October 8, 2015, October 8, 2015, October 13, 2015, October 20, 2015, December 16, 2015 and February 10, 2016; 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.

Any future filings (other than any filings or portions of such reports that are not deemed filed under the Exchange Act in accordance with the Exchange Act and applicable SEC rules, including 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 unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act are also incorporated by reference into this prospectus supplement, including those made after the date of the initial filing

of the registration statement of which this prospectus supplement forms a part, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus supplement, and such future filings will become a part of this prospectus supplement from the date that such filing is made with the SEC. Information in such future filings updates and supplements the information provided in this prospectus supplement. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

To obtain copies of these filings, see Where You Can Find More Information on page S-15 of this prospectus.

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PROSPECTUS

$100,000,000

Common Stock

Warrants

Units

1,500,000 Shares of Common Stock

Offered by the Selling Stockholders

From time to time, we may offer up to $100,000,000 of any combination of the securities described in this prospectus, either individually or in units. The warrants may be exercisable or exchangeable for common stock. In addition, the prospectus provides for the possible resale by certain of our stockholders to be named, from time to time, in one or more offerings, under this prospectus. In the prospectus supplement relating to any sales by the selling stockholders, we will, among other things, identify the number of shares of our common stock that each selling stockholder will be selling. We will not receive any of the proceeds from the sale of shares of our common stock by the selling stockholders.

Each time we or the selling stockholders 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 or the selling stockholders 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 December 24, 2013, the last reported sale price of our common stock on the NYSE MKT LLC was $7.65. 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 4 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 January 22, 2014.

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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 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 prospectus provides for the possible resale by certain of our stockholders to be named, from time to time, in one or more offerings, under this prospectus. We will not receive any proceeds from the sale of securities by the selling stockholders. This prospectus provides you with a general description of the securities we or the selling stockholders may offer. Each time we or the selling stockholders 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. Neither we nor the selling stockholders have authorized anyone to provide you with different information in addition to or different from that contained in this prospectus, any applicable prospectus supplement and any related free writing prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we may authorize to be provided to you. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

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

SUMMARY

This summary highlights selected information from this prospectus or incorporated by reference in this prospectus, and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities contained in the applicable prospectus supplement and any related free writing prospectus, and in the other documents that are incorporated by reference into this prospectus. You

should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Unless otherwise mentioned or unless the context requires otherwise, throughout this prospectus, any applicable prospectus supplement and any related free writing prospectus, the words Ampio, we, us, our, the company or similar references refer to Ampio Pharmaceuticals, Inc. and its subsidiaries on a consolidated basis. References to BioSciences in this prospectus mean DMI BioSciences, Inc., now a wholly-owned subsidiary of ours. References to Life Sciences in this prospectus mean DMI Life Sciences, Inc., which is our predecessor for accounting purposes and a wholly-owned subsidiary of ours. References to Luoxis in this prospectus mean Luoxis Diagnostics, Inc., which is an 80.9% owned subsidiary formed on January 24, 2013 to focus on the development and commercialization of the Oxidation Reduction Potential (ORP) technology platform. References to Vyrix in this prospectus mean Vyrix Pharmaceuticals, Inc., which is a wholly-owned subsidiary formed on November 18, 2013 to focus on our sexual dysfunction business. The term securities refers collectively to our common stock, warrants to purchase common stock, or units or any combination of the foregoing securities; the term selling stockholders refers to certain of our stockholders who may sell their securities under this prospectus and who will be named in a prospectus supplement.

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This prospectus and the information incorporated herein by reference includes trademarks and pending trademarks, such as Optina, Zertane, Ampion, Luoxis, and Vyrix, which are protected under applicable intellectual property laws and are our property or the property of our subsidiaries. This prospectus may also contain trademarks, service marks, copyrights and trade names of other companies which are the property of their respective owners. Solely for convenience, our trademarks and tradenames referred to in this prospectus may appear without the ® or symbols, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights to these trademarks and tradenames.

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

Overview

Ampio Pharmaceuticals, Inc. is a development stage biopharmaceutical company focused primarily on the development of therapies to treat prevalent inflammatory conditions for which there are limited treatment options. Ampio s two lead product candidates in development are Ampion for osteoarthritis of the knee and Optina for diabetic macular edema. We have various other product candidates as well as a diagnostic platform that Ampio is currently developing and a sexual dysfunction portfolio.

Our predecessor, DMI Life Sciences, Inc., or Life Sciences, was incorporated in Delaware in December 2008 and did not conduct any business activity until April 16, 2009, at which time Life Sciences purchased certain assigned intellectual property, business products and tangible property from BioSciences. Life Sciences issued 3,500,000 shares of its common stock to BioSciences, and assumed certain liabilities, as consideration for the assets purchased from BioSciences. The assets Life Sciences acquired from BioSciences had a carrying value of zero, as BioSciences had expensed all of the research and development costs it incurred with respect to the intellectual property purchased by Life Sciences.

In March 2010, Life Sciences was merged with a subsidiary of Chay Enterprises, Inc., a publicly-traded company then traded on the OTC Bulletin Board. Chay Enterprises had minimal operations prior to the time of this merger, and like similar entities, was referred to as a public shell. As a result of this merger, Life Sciences stockholders became the controlling stockholders of Chay Enterprises and the former sole officer and director of Chay Enterprises appointed a majority of our current management team to their present positions.

We were reincorporated in Delaware at that time as Ampio Pharmaceuticals, Inc. and commenced trading on the OTC Bulletin Board as Ampio Pharmaceuticals, Inc. in late March 2010.

On March 23, 2011, Ampio acquired all of the outstanding stock of BioSciences. Its principal asset consisted of the worldwide rights to Zertane, as to which BioSciences held 32 issued patents and 31 pending patent applications. Zertane is a repurposed drug to treat male sexual dysfunction pertaining to premature ejaculation (PE).

In May 2011, our common stock commenced trading on the NASDAQ Capital Market under the symbol AMPE, at which time our common stock ceased trading on the OTC Bulletin Board.

On June 17, 2013, our common stock commenced trading on the NYSE MKT under the symbol AMPE at which time our common stock ceased trading on the NASDAQ.

Corporate Information

Our principal executive offices are located at 5445 DTC Parkway, Suite 925, Greenwood Village, Colorado 80111, 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.

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The Securities We May Offer

We may offer shares of our common stock 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. This prospectus provides you with a general description of the securities we 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 offering price;
- maturity, if applicable;
- redemption, conversion, exercise, or exchange terms, if any;
- 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 may sell the securities directly to investors or to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do 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. 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.

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

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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.

SELLING STOCKHOLDERS

This prospectus also relates to the possible resale by certain of our stockholders, who we refer to in this prospectus as the selling stockholders, of up to 1,500,000 shares of our common stock that were issued and outstanding, or that are issuable upon exercise of options or warrants to acquire common stock that were issued and outstanding, prior to the date of effectiveness of the registration statement of which this prospectus forms a part. The prospectus provides for the possible resale by selling stockholders, from time to time, in one or more offerings, under this prospectus. The selling stockholders originally acquired (or, in the case of issued and outstanding options and warrants, will acquire) the shares of our common stock included in this prospectus through (i) our acquisition transactions with DMI BioSciences, Inc., (ii) our merger transaction in 2010, (iii) certain private financing transactions since 2009, (iv) the exercise of stock options granted during the years from 2010 through 2013 under our 2010 Stock Option and Incentive Plan, as amended, prior to the original date of filing of the registration statement of which this prospectus forms a part, and (v) in connection with our public offering in July 2012.

Information about the selling stockholders, where applicable, including their identities, the amount of shares of common stock owned by each selling stockholder prior to the offering, the number of shares of our common stock to

be offered by each selling stockholder and the amount of common stock to be owned by each selling stockholder after completion of the offering, will be set forth in an applicable prospectus supplement, documents incorporated by reference or in a free writing prospectus we file with the SEC. The applicable prospectus supplement will also disclose whether any of the selling stockholders has held any position or office with, has been employed by or otherwise has had a material relationship with us during the three years prior to the date of the prospectus supplement.

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The selling stockholders may not sell any shares of our common stock pursuant to this prospectus until we have identified such selling stockholders and the shares being offered for resale by such selling stockholders in a subsequent prospectus supplement. However, the selling stockholders may sell or transfer all or a portion of their shares of our common stock pursuant to any available exemption from the registration requirements of the Securities Act.

FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference into it 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, project, plan, assume or other similar expressions, although not all forward-looking statements contain these identifying words. All statements contained in this prospectus and the documents incorporated by reference herein regarding our future strategy, plans and expectations regarding clinical trials, future regulatory approvals, our plans for the 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 are issued or denied by the FDA, the EMEA, or other regulatory agencies;
- 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;

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.

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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 apply 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 forward-looking statements included in this prospectus, 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, and such differences might be significant and materially adverse to our investors. 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 Additional Information and Incorporation of Certain Information by Reference , all of which are accessible on the SEC s website at www.sec.gov.

USE OF PROCEEDS

Except as described in any prospectus supplement or in any related free writing prospectus that we may authorize to be provided to you, the net proceeds received by us from our sale of the securities described in this prospectus will be added to our general funds and will be used for our general corporate purposes. We will not receive any of the proceeds from the sale of shares by any selling stockholders. From time to time, we may engage in additional public or private financings of a character and amount which we may deem appropriate.

PLAN OF DISTRIBUTION

We and the selling stockholders may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We and the selling stockholders may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We and the selling stockholders may distribute securities 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 or the selling stockholders offer and sell securities, 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 or the selling stockholders 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.

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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 or the selling stockholders 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 and the selling stockholders may use underwriters with whom we or they have a material relationship. The prospectus supplement, naming the underwriter, will describe the nature of any such relationship.

We and the selling stockholders 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 and the selling stockholders 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 and the selling stockholders may authorize agents or underwriters to solicit offers by certain purchasers to purchase securities from us or them 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 or the selling stockholders must pay for solicitation of these contracts.

We and the selling stockholders 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 or the selling stockholders 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.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

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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 December 8, 2013, there were 41,998,936 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

Our certificate of incorporation provides that shares of preferred stock may be issued from time to time in one or more series. Our board of directors is authorized to fix the voting rights, if any, designations, powers, preferences, the relative, participating, optional or other special rights and any qualifications, limitations and restrictions thereof, applicable to the shares of each series. Our board of directors will be able to, without stockholder approval, issue preferred stock with voting and other rights that could adversely affect the voting power and other rights of the holders of the common stock and could have anti-takeover effects. The ability of our board of directors to issue preferred stock without stockholder approval could have the effect of delaying, deferring or preventing a change of control or the removal of existing management. We have no preferred stock outstanding at the date hereof. Although we do not currently intend to issue any shares of preferred stock, we cannot assure you that we will not do so in the future.

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:

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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.

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Other than the action, Sunrise Capital, LLC et al. v. Ampio Pharmaceuticals, Inc. et al., described in our Form 8-K dated September 5, 2013, 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 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;

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- 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:

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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.

EXPERTS

The consolidated financial statements of Ampio Pharmaceuticals, Inc. and subsidiaries as of December 31, 2012, 2011, and 2010 and for each of the years in the three-year period ended December 31, 2012, have been incorporated by reference herein from our Annual Report on Form 10-K for the year ended December 31, 2012, 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:

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our Annual Report on Form 10-K for the year ended December 31, 2012, filed on March 6, 2013;

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2013, June 30, 2013 and September 30, 2013, filed on May 3, 2013, August 9, 2013 and November 8, 2013, respectively;

our Current Reports on Form 8-K and 8-K/A (other than portions thereof 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) filed on January 25, 2013, February 15, 2013, March 1, 2013, April 4, 2013, June 7, 2013, July 19, 2013, August 20, 2013, September 5, 2013, September 10, 2013, September 26, 2013, October 4, 2013, October 15, 2013, December 17, 2013 and December 19, 2013.

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, together with all selling stockholders, sell all of the shares covered by this prospectus or the sale of shares by us and the selling stockholders 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., 5445 DTC Parkway, Suite 925, Greenwood Village, Colorado 80111 or call (720) 437-6500.

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Up to $25,000,000

Common Stock

PROSPECTUS SUPPLEMENT

February 10, 2016