

Ampio Pharmaceuticals, Inc.
Form 424B5
August 30, 2016
Table of Contents

**Filed pursuant to Rule 424(b)(5)
Registration No. 333-193096**

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectuses Dated January 22, 2014)

5,000,000 Shares

Common Stock

Warrants to Purchase up to

5,000,000 Shares

We are offering directly to an institutional investor 5,000,000 shares of our common stock, par value \$0.0001 per share, and warrants to purchase up to 5,000,000 shares of our common stock. The common stock and warrants will be sold in units, with each unit consisting of one share of common stock and a warrant to purchase one share of common stock. The warrants have an exercise price of \$1.00 per share. Each unit will be sold to the investor in this offering at a negotiated price of \$0.75 per unit. The shares of common stock and warrants will be issued separately but can only be purchased together in this offering.

Our common stock is listed on NYSE MKT under the symbol AMPE. The last reported sale price of our common stock on the NYSE MKT on August 26, 2016 was \$0.91 per share. There is no established trading market for the warrants and we do not expect a market to develop. In addition, we do not intend to list the warrants on the NYSE MKT, any other national securities exchange or any other nationally recognized trading system.

Investing in our securities involves significant risks. Please read the information contained in or incorporated by reference under the heading Risk Factors beginning on page S-9 of this prospectus supplement, and under similar headings in other documents filed after the date hereof and incorporated by reference into this prospectus supplement and the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is

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

	Per Unit	Total
Offering price	\$ 0.750	\$ 3,750,000
Placement agent fee	\$ 0.045	\$ 225,000
Proceeds, before expenses, to us(1)	\$ 0.705	\$ 3,525,000

(1) The amount of the offering proceeds to us presented in this table does not give effect to any exercise of the warrants being issued in this offering.

Delivery of the shares and warrants will take place on or about September 1, 2016, subject to the satisfaction of certain conditions.

The date of this prospectus supplement is August 29, 2016.

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

	Page
<u>About This Prospectus Supplement</u>	S-1
<u>Where You Can Find Additional Information</u>	S-2
<u>Incorporation of Certain Information By Reference</u>	S-3
<u>Special Note Regarding Forward-Looking Statements</u>	S-4
<u>Summary</u>	S-5
<u>The Offering</u>	S-8
<u>Risk Factors</u>	S-9
<u>Use of Proceeds</u>	S-11
<u>Dilution</u>	S-12
<u>Price Range of Common Stock and Warrants</u>	S-13
<u>Dividend Policy</u>	S-14
<u>Description of Securities</u>	S-15
<u>Plan of Distribution</u>	S-19
<u>Legal Matters</u>	S-20
<u>Experts</u>	S-20
Prospectus	

	Page
<u>About This Prospectus</u>	1
<u>Summary</u>	1
<u>Risk Factors</u>	4
<u>Selling Stockholders</u>	4
<u>Forward-Looking Statements</u>	5
<u>Use of Proceeds</u>	6
<u>Plan of Distribution</u>	6
<u>Description of Capital Stock</u>	8
<u>Description of Warrants</u>	10
<u>Description of Units</u>	11
<u>Legal Matters</u>	12
<u>Experts</u>	12
<u>Where You Can Find Additional Information</u>	12
<u>Incorporation of Certain Information By Reference</u>	12

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

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

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

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

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

No action is being taken in any jurisdiction outside the United States to permit a public offering of the securities or possession or distribution of this prospectus supplement or the accompanying prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement or the accompanying prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement or the accompanying prospectus applicable to that jurisdiction.

Table of Contents

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-3 (File No. 333-193096) under the Securities Act of 1933, as amended, or the Securities Act, with respect to the securities offered by this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus filed as part of the registration statement do not contain all the information set forth in the registration statement and its exhibits and schedules. For further information about us, we refer you to the registration statement and to its exhibits and schedules.

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

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

Table of Contents

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus supplement and the accompanying prospectus. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and later information that we file with the SEC prior to the completion of this offering will automatically update and supersede this information. We incorporate by reference the documents listed below that we have filed with the SEC:

description of our common stock contained in our Registration Statement on Form 8-A, filed on June 6, 2013;

our Annual Report on Form 10-K for the fiscal year ended December 31, 2015, filed on February 26, 2016;

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2016 and June 30, 2016, filed on May 6, 2016 and August 2, 2016, respectively;

our Current Reports on Form 8-K filed on February 10, 2016, March 7, 2016, June 30, 2016 and August 29, 2016; and

our Proxy Statement on Schedule 14A filed on November 12, 2015 (solely to the extent specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2015).

We also incorporate by reference into this prospectus supplement and the accompanying prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, after the date of this prospectus supplement until we sell all of the securities covered by this prospectus supplement and the accompanying prospectus or the sale of securities by us pursuant to this prospectus supplement and the accompanying prospectus is terminated.

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

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

Ampio Pharmaceuticals, Inc.

373 Inverness Parkway, Suite 200,

Edgar Filing: Ampio Pharmaceuticals, Inc. - Form 424B5

Englewood, Colorado 80112

Attention: Chief Financial Officer

Telephone: (720) 437-6500

S-3

Table of Contents

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 expressions. Not all forward-looking statements contain these identifying words. All statements contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein regarding our future strategy, plans and expectations regarding clinical trials, future regulatory approvals, our plans for the manufacturing and commercialization of our products, future operations, projected financial position, potential future revenues, projected costs, future prospects, and results that might be obtained by pursuing management's current plans and objectives are forward-looking statements. Forward-looking statements include, but are not necessarily limited to, those relating to:

our expectations related to the use of proceeds, if any, from this offering;

our need for, and ability to raise, additional capital;

the results and timing of our clinical trials;

the regulatory review process and any regulatory approvals that may be issued or denied by the Food and Drug Administration (FDA), the European Medicines Agency (EMA), or other regulatory agencies;

our manufacturing plans;

our need to secure collaborators to license, manufacture, market and sell any products for which we receive regulatory approval in the future;

the results of our internal research and development efforts; the commercial success and market acceptance of any of our product candidates that are approved for marketing in the United States or other countries;

the safety and efficacy of medicines or treatments introduced by competitors that are targeted to indications which our product candidates have been developed to treat;

the acceptance and approval of regulatory filings;

our current or prospective collaborators' compliance or non-compliance with their obligations under our agreements with them, or decisions by our collaborators to discontinue clinical trials and return product candidates to us;

our plans to develop other product candidates; and

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

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

Table of Contents

SUMMARY

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

Company Overview

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 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.

Table of Contents

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".

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 United States 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 injection clinical investigations 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 PHASE III 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 announced that we had a meeting with the FDA where a single injection clinical trial and a Special Protocol Assessment, or SPA, was recommended by the FDA as the second 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 of 2015, we announced that the FDA had awarded us a SPA for the second PHASE III pivotal trial of Ampion (PIVOT study). The PIVOT study, which included 480 patients, was a randomized, double-blind, saline-controlled, PHASE III clinical study conducted at 20 sites across the US to examine the safety and efficacy of Ampion intra-articular injection in patients with pain due to osteoarthritis of the knee. The clinical stage of osteoarthritis of knee severity is defined by the Kellgren Lawrence scale, or KL. In March 2016, we announced that enrollment in the PIVOT study was complete. The results stating the PIVOT study did not meet its primary endpoint were announced in June 2016. The primary endpoint was the change in WOMAC A pain score at week 12 as compared to saline. Although the PIVOT study did not meet its primary endpoint, it did show a large reduction in pain from Baseline over 12 weeks. Ampion improved (reduced) WOMAC A pain scores significantly over baseline in all KL grades (reductions in pain: KL 2: 52%, KL 3: 36%, and KL 4: 33%). Additional analyses included adverse events, Patient Global Assessment, and responder status defined as 20% improvement in pain at week 12. Ampion was demonstrated to be safe and well-tolerated with no drug-related serious adverse events and an overall adverse event rate that was similar in both the Ampion and saline groups. We observed the largest differentiation between Ampion and saline in the most severe osteoarthritis of the knee patients (KL 4), where no available non-surgical therapy exists. KL 4 patients have been historically excluded from osteoarthritis of the knee trials because of the advanced stage of their condition. We are pleased with the consistent effect Ampion has demonstrated in all of our clinical trials. We are meeting with the FDA in September 2016 to present our data in support of Ampio in the KL 4 population.

In May of 2016, we announced that patient dosing had begun in the exploratory, PHASE I clinical trial evaluating the safety of a single intra-articular injection of Ampion in adults with pain due to osteoarthritis of the hand, specifically of the first carpo-metacarpal joint of the thumb (basal thumb joint). This trial is a randomized, double-blind, placebo-controlled, single-center study in one of the largest hand surgery clinics in the US.

Ampion Manufacturing Facility

In December 2013, we entered into a ten-year lease of a multi-purpose facility containing approximately 19,000 square feet. This facility includes an FDA compliant clean room to manufacture Ampion, research laboratories and our corporate offices.

We moved into our 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 of 2015. We are now producing the FDA required registration batches and have begun to manufacture product that could potentially be used commercially. We believe that these steps could shorten our regulatory timelines and significantly reduce our time to commercialize Ampion. The facility was fully placed in service during the first quarter of 2016. We manufactured the Ampion drug and placebo (saline) for the second PHASE III Ampion trial in our facility.

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.

Table of Contents

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.

Optina Clinical Development

During 2014 and 2015, we conducted the OptimEyes multicenter, placebo-controlled, randomized, dose ranging trial to evaluate the safety and efficacy of oral Optina, which included 355 patients. The trial showed Optina was safe and well tolerated with no drug related adverse events and no differences in side effect rates between placebo and Optina groups. The trial did not meet its primary endpoint for all patients, however we believe we have successfully identified an optimal dose for a body mass index subgroup of patients who are refractory to currently available therapies and also utilize RAS inhibitors as a medication. As more than 70% of all DME patients are utilizing RAS inhibitors to control their blood pressure, we believe this combination of drugs shows promise as a painless, safe and efficacious oral treatment for DME, and a rescue medication following anti-vascular endothelial growth factor therapy failure. These patients showed a +6.2 letter improvement in visual acuity at three months. We presented these results at the World Ophthalmology Congress in February 2016 and at The Association for Research in Vision and Ophthalmology Conference in May 2016. We also plan to present these results at the 49th Annual RETINA Society Meeting in September 2016.

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.ampioharma.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.

S-7

Table of Contents

THE OFFERING

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

Common stock we are offering	5,000,000 shares.
Common stock to be outstanding after this offering	57,016,432 shares.
Warrants we are offering	We are offering warrants to purchase 5,000,000 shares of common stock. Each warrant has an exercise price of \$1.00 per share, is exercisable immediately upon issuance and will expire on September 1, 2021. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of the warrants. There is currently no market for the warrants and none is expected to develop after this offering. We do not intend to list the warrants on any national securities exchange or other trading market. See Description of Securities for additional information.
NYSE MKT Symbol	Our common stock is quoted on the NYSE MKT under the symbol AMPE.
Use of Proceeds	We estimate that the net proceeds from this offering, after payment of estimated offering expenses payable by us, will be approximately \$3.4 million. We intend to use the net proceeds from this offering for general corporate purposes as well as advancing the BLA for Ampion for its future clinical trials. See Use of Proceeds.
Risk Factors	Investing in our securities involves significant risks. Please read the information contained in or incorporated by reference under the heading Risk Factors beginning on page S-9 of this prospectus supplement, and under similar headings in other documents filed after the date hereof and incorporated by reference into this prospectus supplement and the accompanying prospectus.

The number of shares of common stock shown above to be outstanding after this offering is based on 52,016,432 shares outstanding as of June 30, 2016 and excludes:

6,845,832 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2016, at a weighted average exercise price of \$3.78 per share;

Edgar Filing: Ampio Pharmaceuticals, Inc. - Form 424B5

3,441,647 shares of our common stock reserved for future issuance under our 2010 Stock Incentive Plan as of June 30, 2016;

498,576 shares of our common stock issuable upon the exercise of warrants outstanding as of June 30, 2016, at a weighted average exercise price of \$3.24 per share;

5,000,000 shares of our common stock issuable upon the exercise of warrants offered hereby; and

150,000 shares of our common stock issuable upon the exercise of the warrants being granted to the placement agent in this offering (See Plan of Distribution beginning on page S-19 of this prospectus supplement).

S-8

Table of Contents

RISK FACTORS

*Investing in our securities involves a high degree of risk. In addition to the other information contained in this prospectus supplement and in the documents we incorporate by reference, you should carefully consider the risks discussed below and under the heading **Risk Factors** in our Annual Report on Form 10-K for the fiscal year ended December 31, 2015 before making a decision about investing in our securities. The risks and uncertainties discussed below and in our Annual Report on Form 10-K for the fiscal year ended December 31, 2015 are not the only ones facing us. Additional risks and uncertainties not presently known to us may also harm our business. If any of these risks occur, our business, financial condition and operating results could be harmed, the trading price of our common stock could decline and you could lose part or all of your investment.*

Risks Related to Our Common Stock and the Warrants

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

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

The warrants may never have any value.

The warrants comprising part of the units being sold in this offering, which have an exercise price of \$1.00 per whole share of

common stock will expire on September 1, 2021. In the event our common stock price does not exceed the per share exercise price of the warrants during the period when the warrants are exercisable, the warrants will not have any value.

There is no public market for the warrants to purchase common stock being offered in this offering.

There is no established public trading market for the warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply for listing of the warrants on any national securities exchange or other trading market. Without an active market, the liquidity of the warrants will be limited.

Holders of our warrants will have no rights as a common stockholder until such holders exercise their warrants and acquire our common stock.

Until you acquire shares of our common stock upon exercise of your warrants, you will have no rights with respect to the shares of our common stock underlying such warrants. Upon exercise of your warrants, you will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

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

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

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

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

Table of Contents

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

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

Since the offering price per unit of the securities being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the offering price of \$0.75 per unit and attributing no value to the warrants, if you purchase units in this offering, you will suffer immediate and substantial dilution of \$0.46 per share in the net tangible book value of the common stock. In the event that you exercise your warrants, you will experience additional dilution to the extent that the exercise price of those warrants is higher than the book value per share of our common stock. See the section entitled "Dilution" below for a more detailed discussion of the dilution you would incur if you purchase securities in this offering.

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

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

Table of Contents

USE OF PROCEEDS

We estimate that the proceeds from this offering will be approximately \$3.4 million, after deducting estimated offering expenses payable by us. This amount does not include the proceeds that we may receive in connection with any exercise of the warrants issued in this offering. We intend to use the net proceeds from this offering for general corporate purposes as well as advancing the BLA for Ampion for its future clinical trials. We have not determined the amounts we plan to spend on the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds from this offering. Pending application of the net proceeds as described above, we intend to invest the net proceeds of this offering in short-term, investment-grade, interest-bearing securities.

S-11

Table of Contents**DILUTION**

If you purchase units in this offering, you will experience dilution to the extent of the difference between the public offering price of the units (attributing no value to the warrants) and the net tangible book value per share of our common stock immediately after this offering.

Our net tangible book value as of June 30, 2016 was approximately \$13.1 million, or \$0.25 per share of common stock. Net tangible book value per share is equal to our total tangible assets minus total liabilities, all divided by the number of shares of common stock outstanding as of June 30, 2016.

After giving effect to the sale of 5,000,000 units at a price of \$0.75 per unit, and after deducting offering expenses payable by us, and attributing no value to the warrants, our as adjusted net tangible book value would have been approximately \$16.6 million, or approximately \$0.29 per share of common stock, as of June 30, 2016. This represents an immediate increase in net tangible book value of approximately \$0.04 per share to existing stockholders and an immediate dilution of approximately \$0.46 per share to new investors. The following table illustrates this calculation on a per share basis:

Offering price per unit	\$ 0.75
Net tangible book value per share as of June 30, 2016	\$ 0.25
Increase in net tangible book value per share attributable to new investors	\$ 0.04
As adjusted net tangible book value per share after giving effect to this offering	\$ 0.29
Dilution per share to investors in this offering	\$ 0.46

The number of shares of common stock shown above to be outstanding after this offering is based on 52,016,432 shares outstanding as of June 30, 2016 and excludes:

6,845,832 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2016, at a weighted average exercise price of \$3.78 per share;

3,441,647 shares of our common stock reserved for future issuance under our 2010 Stock Incentive Plan as of June 30, 2016;

498,576 shares of our common stock issuable upon the exercise of warrants outstanding as of June 30, 2016, at a weighted average exercise price of \$3.24 per share;

5,000,000 shares of our common stock issuable upon the exercise of warrants offered hereby; and

150,000 shares of our common stock issuable upon the exercise of the warrants being granted to the placement agent in this offering (See Plan of Distribution beginning on page S-19 of this prospectus supplement). The above illustration of dilution per share to investors participating in this offering assumes no exercise of outstanding options to purchase our common stock or outstanding warrants to purchase shares of our common stock. The exercise of outstanding options and warrants having an exercise price less than the offering price will increase dilution to new investors. In addition, we may choose to raise additional capital depending on market conditions, our capital requirements and strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

S-12

Table of Contents**PRICE RANGE OF COMMON STOCK**

On June 17, 2013, our common stock began trading on the NYSE MKT under the ticker symbol AMPE . It was previously quoted on the NASDAQ Capital Market under the same ticker symbol AMPE . The following table sets forth the high and low last reported sale price information for our common stock for the periods indicated.

	High	Low
Year ending December 31, 2016		
1st Quarter	\$ 3.31	\$ 1.90
2nd Quarter	\$ 4.21	\$ 1.29
3rd Quarter (through August 26, 2016)	\$ 1.31	\$ 0.87
Year ended December 31, 2015		
1st Quarter	\$ 7.60	\$ 3.68
2nd Quarter	\$ 7.38	\$ 1.79
3rd Quarter	\$ 3.12	\$ 2.00
4th Quarter	\$ 3.28	\$ 2.51
Year ended December 31, 2014		
1st Quarter	\$ 9.73	\$ 5.70
2nd Quarter	\$ 8.35	\$ 5.44
3rd Quarter	\$ 8.59	\$ 3.33
4th Quarter	\$ 4.16	\$ 3.25
Year ended December 31, 2013		
1st Quarter	\$ 4.89	\$ 3.65
2nd Quarter	\$ 6.72	\$ 4.63
3rd Quarter	\$ 7.79	\$ 5.27
4th Quarter	\$ 10.55	\$ 6.62

On August 29, 2016, the last reported sale price for our common stock on the NYSE MTK was \$0.91 per share. As of August 29, 2016, there were of record approximately 267 holders of our common stock.

Table of Contents

DIVIDEND POLICY

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

S-14

Table of Contents

DESCRIPTION OF SECURITIES

In this offering, we are offering 5,000,000 shares of common stock and warrants to purchase up to 5,000,000 shares of common stock. This prospectus supplement also relates to the offering of shares of our common stock upon the exercise, if any, of the warrants issued in this offering.

Common Stock

Pursuant to our certificate of incorporation, we are currently authorized to issue 100,000,000 shares of common stock, par value \$0.0001 per share. As of June 30, 2016, there were 52,016,432 shares of our common stock outstanding.

The material terms and provisions of our common stock are described under the caption Description of Capital Stock starting on page 8 of the accompanying prospectus.

Warrants

The material terms and provisions of the warrants to purchase 5,000,000 shares of common stock being offered pursuant to this prospectus supplement and the accompanying prospectus are summarized below. This summary is subject to and qualified in its entirety by the form of warrant, which will be provided to the investor in this offering and will be filed on a Current Report on Form 8-K in connection with this offering.

General Terms of the Warrants

The warrants to be issued in this offering represent the rights to purchase up to 5,000,000 shares of common stock at an initial exercise price of \$1.00 per share. Each warrant may be exercised at any time beginning September 1, 2016 and from time to time thereafter through and including the fifth year anniversary of the initial exercise date.

Exercisability

The warrants will be exercisable upon issuance and will expire on the five-year anniversary of issuance. The warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and payment in full of the exercise price within one trading day in available funds for the number of shares of common stock purchased upon such exercise. If a registration statement registering the resale of the shares of common stock underlying the warrants under the Securities Act of 1933, as amended, or the Securities Act, is not available, the holder may, in its sole discretion, elect to exercise the warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the warrant certificate. No fractional shares of common stock will be issued in connection with the exercise of a warrant. In lieu of fractional shares, we will issue a number of shares of our common stock rounded up to the nearest whole number.

Failure to Timely Deliver Shares

If we fail to deliver to the holder a certificate representing shares issuable upon exercise of a warrant or to credit the holder's balance account with Depository Trust Company for such number of shares of common stock to which the holder is entitled upon the holder's exercise of the warrant, in each case, by the delivery date set forth in the warrant, and if on or after such date the holder purchases the shares of our common stock to deliver in satisfaction of a sale by the holder of the underlying warrant shares that the holder anticipated receiving from us, then, within three business days of receipt of the holder's request, we, at the holder's discretion, will either (i) pay cash to the holder in an amount

equal to the holder's total purchase price (including brokerage commissions, if any) for the shares of common stock purchased, or the buy-in price, at which point our obligation to deliver the underlying common stock will terminate, or (ii) promptly honor our obligation to deliver to the holder a certificate or certificates representing the underlying common stock or credit the holder's balance account with Depository Trust Company and pay cash to the holder in an amount equal to the excess (if any) of the buy-in price over the product of (A) the number of shares of common stock, times (B) the closing bid price on the date of exercise.

Exercise Limitation

In general, a holder will not have the right to exercise any portion of the warrant if the holder (together with its affiliates) would beneficially own in excess of 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the

Table of Contents

exercise, as such percentage ownership is determined in accordance with the terms of the warrant certificate. However, any holder may increase or decrease such percentage to any other percentage not in excess of 9.99% upon notice to us, provided that any increase in this limitation will not be effective until 61 days after such notice from the holder to us and such increase or decrease will apply only to the holder providing such notice.

Certain Adjustments

The exercise price and the number of shares of common stock purchasable upon the exercise of the warrants are subject to adjustment upon the occurrence of specific events, including sales of additional shares of common stock, stock dividends, stock splits, combinations and reclassifications of our common stock.

Transferability

Subject to applicable laws, the warrants may be offered for sale, sold, transferred or assigned. There is currently no trading market for the warrants and a trading market is not expected to develop.

Fundamental Transactions

If a fundamental transaction (as defined below) occurs, then the successor entity will succeed to, and be substituted for us, and may exercise every right and power that we may exercise and will assume all of our obligations under the warrants with the same effect as if such successor entity had been named in the warrant itself. Additionally, upon consummation of a fundamental transaction pursuant to which holders of shares of our common stock are entitled to receive securities or other assets with respect to or in exchange for shares of our common stock, we will make appropriate provision to insure that the holder will thereafter have the right to receive upon an exercise of the warrant at any time after the consummation of the fundamental transaction but prior to the expiration date of the warrant, in lieu of shares of our common stock (or other securities, cash, assets or other property) purchasable upon the exercise of the warrant prior to such fundamental transaction, such shares of stock, securities, cash, assets or any other property whatsoever (including warrants or other purchase or subscription rights) which the holder would have been entitled to receive upon the happening of such fundamental transaction had the warrant been exercised immediately prior to such fundamental transaction. If holders of our common stock are given a choice as to the securities, cash or property to be received in a fundamental transaction, then the holder shall be given the same choice as to the consideration it receives upon any exercise of the warrant following such fundamental transaction. These provisions apply similarly and equally to successive fundamental transactions and other corporate events described in the warrant certificate and will be applied without regard to any limitations on the exercise of the warrant. In the event of certain fundamental transactions, at the request of the holder, we or the successor entity shall purchase the unexercised portion of the warrant from the holder by paying to the holder, within second trading days after such request (or, if later, on the effective date of the fundamental transaction), cash in an amount equal to the Black-Scholes Value (as defined below) of the remaining unexercised portion of the warrant on the date of such fundamental transaction.

Definitions

Black-Scholes Value means the value of the unexercised portion of the warrant remaining on the date of the Holder's request to us to repurchase the warrant (the Request Date), which value is calculated using the Black-Scholes Option Pricing Model obtained from the `OV` function on Bloomberg utilizing:

- (i) an underlying price per share equal to the greater of:

- (1) the highest closing sale price of our common stock during the period beginning on the trading day immediately preceding the announcement of the applicable Fundamental Transaction (or the consummation of the applicable Fundamental Transaction, if earlier) and ending on the trading day of the Request Date; and
 - (2) the sum of the price per share being offered in cash in the applicable Fundamental Transaction (if any) plus the value of the non-cash consideration being offered in the applicable Fundamental Transaction (if any);
- (ii) a strike price equal to the exercise price in effect on the Request Date;
- (iii) a risk-free interest rate corresponding to the U.S. Treasury rate for a period equal to the greater of:
- (1) the remaining term of the warrant as of the Request Date; and
 - (2) the remaining term of this Warrant as of the date of consummation of the applicable Fundamental Transaction or as of the Request Date if such request is prior to the date of the consummation of the applicable Fundamental Transaction;

Table of Contents

- (iv) a zero cost of borrow; and

- (v) an expected volatility equal to the greater of 75% and the 30 day volatility obtained from the HVT function on Bloomberg (determined utilizing a 365 day annualization factor) as of the Trading Day immediately following the earliest to occur of:
 - (1) the public disclosure of the applicable Fundamental Transaction;
 - (2) the consummation of the applicable Fundamental Transaction; and
 - (3) the date on which the Holder first became aware of the applicable Fundamental Transaction.

Fundamental Transaction means:

- (i) that we shall, directly or indirectly:
 - (1) consolidate or merge with or into (whether or not we are the surviving corporation) another entity;
 - (2) sell, assign, transfer, convey or otherwise dispose of all or substantially all of our properties or assets; or
 - (3) make, or allow one or more entities to make (the Subject Entities), or allow us to be subject to or have our common stock be subject to or party to one or more Subject Entities making, a purchase, tender or exchange offer that is accepted by the holders of at least either:
 - (x) 50% of our outstanding shares;
 - (y) 50% of our outstanding shares calculated as if any shares of our common stock held by the Subject Entities making such purchase, tender or exchange offer were not outstanding; or
 - (z) such number of shares of our common stock such that the Subject Entities making such purchase, tender or exchange offer, become collectively the beneficial owners (as defined in Rule 13d-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act) of at least 50% of our outstanding common stock; or

(4)

consummate a stock or share purchase agreement or other business combination (including, without limitation, a reorganization, recapitalization, spin-off or scheme of arrangement) with one or more Subject Entities whereby all such entities, individually or in the aggregate, acquire, either:

(x) at least 50% of the outstanding shares our common stock;

(y) at least 50% of our outstanding shares of common stock calculated as if any shares of our common stock held by all the Subject Entities making or party to, or affiliated with any Subject Entity making or party to, such stock purchase agreement or other business combination were not outstanding; or

(z) such number of shares of our common stock such that the Subject Entities become collectively the beneficial owner of at least 50% of our outstanding common stock; or

(5) reorganize, recapitalize or reclassify our common stock;

(ii) we shall, directly or indirectly, allow any Subject Entity individually or the Subject Entities in the aggregate to be or become the beneficial owner, directly or indirectly, whether through acquisition, purchase, assignment, conveyance, tender, tender offer, exchange, reduction in outstanding shares of our common stock, merger, consolidation, business combination, reorganization, recapitalization, spin-off, scheme of arrangement, reorganization, recapitalization or reclassification or otherwise in any manner whatsoever, of either:

(A) at least 50% of the aggregate ordinary voting power represented by issued and outstanding common stock;

Table of Contents

- (B) at least 50% of the aggregate ordinary voting power represented by issued and outstanding common stock not held by all such Subject Entities as of the date of the warrant calculated as if any shares of our common stock held by all such Subject Entities were not outstanding;

 - (C) a percentage of the aggregate ordinary voting power represented by issued and outstanding shares of our common stock or other of our equity securities sufficient to allow such Subject Entities to effect a statutory short form merger or other transaction requiring our shareholders to surrender their shares of common stock without approval of our shareholders;
- (ii) directly or indirectly, the issuance of or the entering into any other instrument or transaction structured in a manner to circumvent, or that circumvents, the intent of this definition in which case this definition shall be construed and implemented in a manner otherwise than in strict conformity with the terms of this definition to the extent necessary to correct this definition or any portion of this definition which may be defective or inconsistent with the intended treatment of such instrument or transaction.

Table of Contents

PLAN OF DISTRIBUTION

We have entered into a securities purchase agreement with an institutional investor pursuant to which we will sell to such purchaser 5,000,000 shares of our common stock and warrants to purchase up to 5,000,000 shares of our common stock. The common stock and warrants will be sold in units, with each unit consisting of one share of common stock and a warrant to purchase one share of common stock. The warrants have an exercise price of \$1.00 per share of common stock. Each unit will be sold to the investor in this offering at a negotiated price of \$0.75 per unit. The shares of common stock and warrants will be issued separately but can only be purchased together in this offering. We negotiated the prices of the securities offered in this offering with the investor. The factors considered in determining the price included the recent market price of our common stock, the general condition of the securities market at the time of this offering, the history of, and the prospects for, the industry in which we compete, our past and present operations, and our prospects for future revenues.

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

We will deliver the shares of common stock being issued to the investor electronically upon receipt of investor funds for the purchase of the shares of our common stock and warrants offered pursuant to this prospectus supplement. The warrants will be issued in registered physical form. We currently anticipate that the closing of the sale of the shares of common stock and warrants offered pursuant to this prospectus supplement will take place, and we expect to deliver the shares of our common stock and warrants that are purchased, on or about September 1, 2016. The obligations of the investor to close this offering are subject to certain conditions, including the absence of any material adverse change in our business and the receipt of customary letters and certificates.

We estimate the total offering expenses of this offering that will be payable by us will be approximately \$100,000, which include legal and printing costs and various other fees and. At the closing, we will mail the warrants and the Depository Trust Company will credit the common stock directly to invest at the address set forth in the securities purchase agreement.

We have agreed to reimburse the purchasers for certain specified expenses, including the fees and disbursements of its legal counsel, in an amount not to exceed \$30,000.

Financial West Group, member FINRA/SIPC, (Financial West Group) is acting as our placement agent in this offering and will receive a placement agent fee equal to 6.0% of the aggregate offering proceeds. As part of Financial West Group s compensation for this offering, we have agreed to issue to Financial West Group, or its designees, warrants to purchase a number of shares of our common stock, par value \$0.0001 per share, equal to an aggregate of 3.0% of the shares of common stock included as a component of the units sold in the offering. This warrant will have an exercise price equal to \$0.9375 per share. Financial West Group s warrant is exercisable upon issuance and will be exercisable for five years following the date of this prospectus. Financial West Group s warrant is not redeemable by us, and allows for cashless exercise. Pursuant to the rules of the Financial Industry Regulatory Authority, Inc., or FINRA, and in particular Rule 5110(g)(1), the representative s warrant (and underlying shares of our common stock) may not be sold, transferred, assigned, pledged, or hypothecated, or the subject of any hedging, short sale, derivative, put or call transaction that would result in the effective disposition of the securities by any person for a period of 180 days immediately following the date of this prospectus; provided, however, Financial West Group s warrant (and underlying shares) may be transferred to its officers or directors as long as the warrant (and underlying shares) remain subject to the lockup.

Financial West Group's warrant contains anti-dilution terms that allows Financial West Group to receive more shares or exercise at a lower price than originally agreed to upon at the time of the offering, provided that the public stockholders are proportionally affected by a stock split, stock dividend, or other similar event. Financial West Group's warrant will not provide for it to accrue cash dividends prior to the exercise or conversion of the warrant.

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

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

Table of Contents

LEGAL MATTERS

The validity of the securities offered hereby has been passed upon for us by Goodwin Procter LLP, New York, New York.

EXPERTS

The consolidated balance sheets of Ampio Pharmaceuticals, Inc. as at December 31, 2015 and 2014 and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2015 and the related financial statement schedule have been audited by EKS&H LLLP, independent registered public accounting firm, as stated in their report which is incorporated herein by reference from the Annual Report on Form 10-K for the fiscal year ended December 31, 2015. Such consolidated financial statements and schedule have been incorporated in reliance upon the report of such experts in accounting and auditing.

S-20

Table of Contents

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.

Table of Contents

TABLE OF CONTENTS

	Page
<u>ABOUT THIS PROSPECTUS</u>	1
<u>SUMMARY</u>	1
<u>RISK FACTORS</u>	4
<u>SELLING STOCKHOLDERS</u>	4
<u>FORWARD-LOOKING STATEMENTS</u>	5
<u>USE OF PROCEEDS</u>	6
<u>PLAN OF DISTRIBUTION</u>	6
<u>DESCRIPTION OF CAPITAL STOCK</u>	8
<u>DESCRIPTION OF WARRANTS</u>	10
<u>DESCRIPTION OF UNITS</u>	11
<u>LEGAL MATTERS</u>	12
<u>EXPERTS</u>	12
<u>WHERE YOU CAN FIND ADDITIONAL INFORMATION</u>	12
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	12

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, utilizing a shelf registration process. Under this shelf registration process, we may offer shares of our common stock 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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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:

Table of Contents

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.

Table of Contents

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;

Table of Contents

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:

Table of Contents

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:

Table of Contents

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.ampioharma.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.

Table of Contents