

Ampio Pharmaceuticals, Inc.
Form 424B5
August 08, 2018
Table of Contents

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

This preliminary prospectus supplement and the accompanying prospectus relate to an effective registration statement under the Securities Act of 1933, but the information in this prospectus supplement is not complete and may be changed. This prospectus supplement and the accompanying prospectus are not an offer to sell the securities and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

PRELIMINARY PROSPECTUS SUPPLEMENT (Subject to Completion, dated August 8, 2018)

(To Prospectus Dated April 20, 2017)

Shares Common Stock

Warrants to Purchase up to

Shares of Common Stock

We are offering _____ shares of our common stock, par value \$0.0001 per share, and warrants to purchase up to _____ shares of our common stock pursuant to this prospectus supplement and the accompanying prospectus. The shares of common stock and warrants will be issued separately. Each share of common stock is being sold together with a warrant to purchase _____ shares of common stock.

The warrants will have a term of five years, commencing six months after the date of issuance, and have an exercise price of \$ _____ per share. 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 American under the symbol AMPE. The last reported sale price of our common stock on the NYSE American on August 7, 2018 was \$2.86 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 NYSE American, 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-15 of this prospectus supplement, and under similar headings in other documents filed after the date hereof and incorporated by reference into this prospectus supplement and the accompanying prospectus.

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

	Per Share and Accompanying Warrant	Total
Offering price	\$	\$
Underwriting discount and commissions(1)	\$	\$
Proceeds, before expenses, to us(2)	\$	\$

(1) We have agreed to reimburse the underwriter for certain expenses. See **Underwriting** for a description of the compensation payable to the underwriter.

(2) 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.

The underwriter expects to deliver the shares and warrants against payment in New York, New York on or about August , 2018.

Canaccord Genuity

The date of this prospectus supplement is August , 2018.

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-6
<u>The Offering</u>	S-13
<u>Risk Factors</u>	S-15
<u>Use of Proceeds</u>	S-18
<u>Dilution</u>	S-19
<u>Price Range of Common Stock</u>	S-20
<u>Dividend Policy</u>	S-21
<u>Description of Securities</u>	S-22
<u>Certain U.S. Federal Income Tax Considerations</u>	S-26
<u>Underwriting</u>	S-33
<u>Legal Matters</u>	S-38
<u>Experts</u>	S-38
Prospectus	

	Page
<u>About This Prospectus</u>	1
<u>Summary</u>	2
<u>Risk Factors</u>	5
<u>Forward-Looking Statements</u>	5
<u>Ratio of Earnings to Combined Fixed Charges and Preferred Stock Dividends</u>	7
<u>Use of Proceeds</u>	8
<u>Selling Stockholders</u>	9
<u>Plan of Distribution</u>	11
<u>Description of Capital Stock</u>	14
<u>Description of Debt Securities</u>	19
<u>Description of Warrants</u>	26
<u>Description of Units</u>	27
<u>Legal Matters</u>	28
<u>Experts</u>	28
<u>Where You Can Find Additional Information</u>	28
<u>Incorporation of Certain Information By Reference</u>	28

Table of Contents

ABOUT THIS PROSPECTUS 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. 333-217094) under the Securities Act of 1933, as amended, or the Securities Act, with respect to the securities offered by this prospectus supplement and the accompanying prospectus. This prospectus supplement and the accompanying prospectus filed as part of the registration statement do not contain all the information set forth in the registration statement and its exhibits and schedules. For further information about us, we refer you to the registration statement and to its exhibits and schedules.

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

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

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, 2017, filed on March 6, 2018;

our Quarterly Report on Form 10-Q for the quarter ended March 31, 2018, filed on May 10, 2018; and

our Current Reports on Form 8-K filed on January 8, 2018, April 16, 2018 and August 7, 2018.

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

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

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

Ampio Pharmaceuticals, Inc.

373 Inverness Parkway, Suite 200,

Englewood, Colorado 80112

Attention: Chief Financial Officer

Telephone: (720) 437-6500

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, 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 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 U.S. Food and Drug Administration, the European Medicines Agency or other regulatory agencies;

our manufacturing plans;

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

the results of our internal research and development efforts;

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

the safety and efficacy of medicines or treatments introduced by competitors that are targeted to indications which our product candidates are being 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

S-4

Table of Contents

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

S-5

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

We are a biopharmaceutical company focused primarily on the development of therapies to treat prevalent inflammatory conditions such as severe osteoarthritis of the knee joint and diabetic macular edema, for which there are limited effective treatment options.

Background

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

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

Business Overview

Our Product Pipeline

AMPION

Ampion for Osteoarthritis and Other Inflammatory Conditions

Ampion is the < 5 kDa ultrafiltrate of 5% Human Serum Albumin, or HSA, a biologic approved by the U.S. Food and Drug Administration, or FDA. Ampion is a non-steroidal, low molecular weight, anti-inflammatory biologic, which has the potential to be used in a wide variety of acute and chronic inflammatory conditions, as well as immune-mediated diseases. Ampion and its known components have demonstrated a broad spectrum of anti-inflammatory and immune modulatory activity which support the mechanism of action. We have published several scientific papers and peer-reviewed publications on the mechanism of Ampion.

We are currently developing Ampion as an intra-articular injection to treat the signs and symptoms of severe osteoarthritis of the knee, or OAK. Osteoarthritis is a growing condition in the United States and symptomatic OAK is expected to impact approximately 1 in 2 Americans. OAK is a progressive disease characterized by gradual degradation and loss of cartilage due to inflammation of the soft tissue and bony structures of the knee joint. Progression of the most severe form of OAK leaves patients with little to no treatment options other than a

S-6

Table of Contents

total knee arthroplasty. The FDA has stated that severe OAK is an unmet medical need and there are currently limited licensed therapies for this indication.

We have conducted multiple clinical trials in the development of Ampion that have included over 2,000 patients.

Market Opportunity

Osteoarthritis, or OA, is the most common form of arthritis, affecting over 100 million people in the United States with over 48 million people suffering from osteoarthritis of the knee. It is a progressive disorder of the joint involving degradation of the intra-articular cartilage, joint lining, ligaments, and bone. The incidence of developing osteoarthritis of the knee over a lifetime is approximately 45%. Certain risk factors in conjunction with natural wear and tear lead to the breakdown of cartilage. Osteoarthritis is caused by inflammation of the soft tissue and bony structures of the joint, which worsens over time and leads to progressive thinning of articular cartilage. Other progressive effects include narrowing of the joint space, synovial membrane thickening, osteophyte formation and increased density of subchondral bone. The global osteoarthritis of the knee market currently addresses moderate to moderately severe OA and is over \$3.0 billion. We believe that this market does not account for the underserved severely diseased patients. The global demand for osteoarthritis of the knee treatment is expected to be fueled by aging demographics and increased awareness of treatment options. Despite the size and growth of the osteoarthritis of the knee market, only a few treatment options currently exist, especially in the severely diseased patient population.

Competition

The currently available, non-surgical treatments for osteoarthritis of the knee include oral non-steroidal anti-inflammatory agents, opioids, pain patches, intra-articular, or IA, corticosteroids injections, and IA hyaluronic acid, or HA, injections. In May 2017, the Journal of the American Medical Association released a study from Tufts Medical Center and Boston University School of Public Health finding that the use of intra-articular triamcinolone compared with intra-articular saline resulted in greater cartilage volume loss, with no significant difference in knee pain severity between treatment groups. As a result, the research concluded that the results did not support use of triamcinolone for individuals with symptomatic OAK. In May 2013, the American Academy of Orthopaedic Surgeons, or AAOS, issued its second edition of clinical practice guidelines for the treatment of osteoarthritis of the knee. The AAOS was unable to recommend for or against the use of intra-articular corticosteroid injections as studies designed to indicate efficacy were inconclusive. Further, the AAOS was also unable to recommend for or against the use of acetaminophen, opioids, or pain patches as the efficacy studies in this area were also inconclusive. Most importantly, the AAOS does not recommend (with a strong strength of recommendation) the use of hyaluronic acid injections as, in the AAOS assessment, the clinical evidence does not support their use. This clinical practice guideline underscores a pervasive unmet need in the treatment of osteoarthritis of the knee given few accepted and available treatments. We believe Ampion is a novel treatment option that, if approved, would be the first non-steroidal, non-opioid, non-hyaluronic-based intra-articular treatment available for the treatment of pain due to severe osteoarthritis of the knee.

Clinical Development Pathway

In December 2017, we reported positive results for both the primary and secondary endpoints of our confirmatory single injection Phase III clinical trial of 168 patients, which we also refer to as the AP-003-C trial. The 12-week study evaluated the responder rate of Ampion-treated patients as defined by the Osteoarthritis Research Society International (OARSI) Standing Committee for Clinical Trials Response Criteria Initiative (OMERACT), which included pain, function, and patient global assessment in support of a label for the treatment of the signs and symptoms of severe OAK. Ampion met its primary endpoint with 71% of Ampion treated

S-7

Table of Contents

patients meeting the OMERACT-OARSI responder criteria, which exceeds the physician reported threshold of 30% for a meaningful treatment in severe osteoarthritis of the knee. Responders experienced, on average, a 53% decrease in pain as measured by WOMAC A and a 50% improvement in function as measured by WOMAC C and a 45% improvement in quality of life as measured by Patient Global Assessment (PGA). In the secondary endpoints, Ampion-treated patients achieved statistical significance in a composite endpoint of pain and function from baseline in both categories at 12 weeks, which was supported by an increase in quality of life as measured by PGA. When treated with Ampion, patients experienced significant improvement in a composite endpoint of pain and function compared to all severely diseased saline-treated patients in historical Ampion Phase III clinical trials. We believe that this data supports Ampion's ability to address an unmet medical need and provide patients with a meaningful, non-steroidal, non-opioid, non-hyaluronic-based treatment that improves pain, function and quality of life.

In late 2017, we announced publication of an integrated analysis of 417 severely diseased OAK patients, which we believe to be the largest study treating this patient population, as a feature article in *Orthopedics*, an international peer-reviewed journal. The publication detailed the safety and tolerability of a single intra-articular injection of Ampion into the knee and demonstrated that patients are significantly more likely to respond to treatment with Ampion with a longer duration of response compared to saline. This data suggests that Ampion can potentially satisfy an unmet medical need for a population with few therapeutic treatment options and a debilitating symptomatic disease.

Additionally, we announced the beginning of an Open Label Extension, or OLE, study of the AP-003-C trial. The OLE study offers patients an opportunity to receive repeat injections of Ampion after they have completed the Phase III clinical trial. The OLE study is intended to address the regulatory requirements to support an expanded commercial label for repeat administration of Ampion.

We also intend to study Ampion for therapeutic applications in addition to severe osteoarthritis of the knee. We may engage development partners to study Ampion in various conditions including: (i) acute and chronic inflammatory conditions; (ii) degenerative joint diseases other than severe osteoarthritis of the knee; (iii) respiratory disorders and (iv) osteoarthritis of the hand. Based on the continuing evaluation, we are also studying Ampion's effects on cellular behavior to indicate potential effects on disease modification across multiple conditions. If successful, we believe that 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 medical needs.

Regulatory Update

As a pharmaceutical company that operates in the United States, we are subject to extensive regulation by the FDA and other federal, state, and local regulatory agencies. The Federal Food, Drug, and Cosmetic Act, the Public Health Service Act and FDA's implementing regulations set forth, among other things, requirements for the testing, development, manufacture, quality control, safety, effectiveness, approval, labeling, storage, record keeping, reporting, distribution, import, export, advertising and promotion of our product candidates. Although the discussion below focuses on regulation in the United States, because that is currently our primary focus, we anticipate seeking approval for, and marketing, our products in other countries in the future. Generally, our activities in other countries would be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences.

With respect to FDA review of Ampion and our completed and ongoing clinical trials, including the AP-003-A and AP-003-C trials, we have been and expect to continue to be engaged in meetings and correspondence with the FDA about the product, its manufacturing, and the preclinical and clinical testing necessary to support Ampion's safety and efficacy. We met with the FDA in July 2018 and have received a letter

S-8

Table of Contents

in response thereto. In the letter, the FDA stated that it considers the AP-003-A trial to be an adequate and well-controlled clinical trial that provides evidence of effectiveness of Ampion and can contribute to the substantial evidence of effectiveness necessary for approval of a Biologics License Application, or BLA, but that as a single trial the AP-003-A study alone does not appear to provide sufficient evidence of effectiveness to support a BLA. Despite our belief that the APC-003-C trial design was based on FDA guidance and feedback and consistent with FDA precedent for similar products (in intended use, in origin, and in regulatory pathway), which we reiterated with the FDA multiple times, the FDA does not consider the AP-003-C trial to be an adequate and well-controlled clinical trial. The FDA recommended that we perform an additional randomized trial with a concurrent control group and that we request a Special Protocol Assessment to obtain FDA concurrence of the trial design before beginning the study. We plan to continue to discuss with the FDA the necessity of conducting this additional trial, as we believe the current body of data is sufficient to submit the BLA. Please see the section of this prospectus supplement entitled Risk Factors. The FDA is requiring an additional clinical trial of Ampion for OAK.

Table of Contents

We will also continue to address with the FDA the validation of manufacturing processes and controls for the submission of a BLA for Ampion.

Ampion Manufacturing Facility

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

We moved into this manufacturing facility in the summer of 2014. Since that time, we have implemented a quality system, validated the facility for human-use products and produced Ampion. We presented on single use technology in manufacturing at the 24th Annual Aseptic Processing Technology Conference for the International Society for Pharmaceutical Engineers in February of 2015. We are now in the process of producing the FDA required registration batches of Ampion. The facility was placed in service during the first quarter of 2016. In our facility, we manufactured Ampion and the placebo (saline) for the PIVOT and AP-003-C trials.

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. Macular edema is the most common form of non-proliferative diabetic retinopathy. In diabetic macular edema, prolonged hyperglycemia compromises endothelial cell linkage leading to vascular permeability. The leakage of fluid, solutes, proteins and immune cells cause the macula to swell and thicken. This leads to damage of the central retinal tissue and can significantly impair sharp central vision. 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 the membrane-associated androgen, steroid binding globulin, and calcium channel receptors. At lower concentrations, danazol binds to androgen and steroid binding globulin receptors stimulating the formation of a cortical actin ring. At higher concentrations, activation of the calcium channels shifts the balance towards stress fiber formation and increases vascular permeability.

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

Market Opportunity

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

macular edema, prolonged hyperglycemia compromises endothelial cell linkage

S-10

Table of Contents

leading to vascular permeability. The leakage of fluid, solutes, proteins and immune cells cause the macula to swell and thicken. This leads to damage of the central retinal tissue and can significantly impair sharp central vision. The prevalence of Type 1 and Type 2 diabetes is 11.3% of the population above the age of 20, with an annual incidence of 1.9 million cases in the United States alone. In this population, the prevalence of diabetic macular edema is estimated at 30% of patients inflicted by the disease for 20 years or more.

Competition

There are no orally administered treatments for DME currently available nor to our knowledge are any being tested in clinical trials. The current standard of care in the United States for the treatment of DME is laser photocoagulation. The first and only approved therapy in the United States is intravitreal ranibizumab injections. Ranibizumab belongs to a therapeutic class inhibiting vascular endothelial growth factor, or anti-VEGF. It is important to note that there is significant competition from off-label anti-VEGF treatment of DME from bevacizumab. Iluvien (fluocinolone acetonide micro-insert intravitreal implant) and Dexamethasone have been approved in the United States for DME.

Clinical Development Pathway

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

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

While Optina shows promise, we are currently focusing our resources and clinical development efforts on Ampion to treat severe osteoarthritis of the knee, our highest priority. We plan to explore partnerships and/or development agreements related to Optina, pending further progress on Ampion related to severe osteoarthritis of the knee.

Table of Contents

Financial Update

As of June 30, 2018, we had cash and cash equivalents of approximately \$4.7 million as compared to approximately \$7.5 million as of March 31, 2018.

Corporate Information

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

Our principal executive offices are located at 373 Inverness Parkway, Suite 200, Englewood, Colorado 80112, and our telephone number is (720) 437-6500. Additional information about us is available on our website at www.ampiopharma.com. The information contained on or that may be obtained from our website is not, and shall not be deemed to be, a part of this prospectus supplement.

The 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 warrants, see the Description of Securities section in this prospectus supplement and the Description of Capital Stock section in the accompanying prospectus.

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-14 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 86,011,751 shares outstanding as of March 31, 2018 and excludes:

6,849,165 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2018, at a weighted average exercise price of \$2.81 per share;

S-13

Table of Contents

3,042,262 shares of our common stock reserved for future issuance under our 2010 Stock Incentive Plan as of March 31, 2018;

7,647,744 shares of our common stock issuable upon the exercise of warrants outstanding as of March 31, 2018 (excluding the warrants offered hereby), at a weighted average exercise price of \$0.93 per share; and

shares of common stock issuable upon exercise of warrants to be issued in this offering.

Unless otherwise indicated, all information in this prospectus supplement assumes that none of the warrants issued in this offering are exercised.

S-14

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, 2017 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, 2017 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, the Warrants, this Offering and Our Business

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, which have an exercise price of \$ per whole share of common stock, will expire five years after they are initially exercisable. 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 American.

Market conditions may result in volatility in the level of, and fluctuations in, market prices of stocks generally and, in turn, the price of our common stock. 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.

S-15

Table of Contents

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

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

In the future, we may sell additional shares of our common stock to raise capital or issue stock in connection with acquisitions. In addition, a substantial number of shares of our common stock are reserved for issuance upon the exercise of warrants 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.

Because the price per share of our common stock 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. If you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$ 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.

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

Our common stock trades on the NYSE American. The NYSE American imposes various quantitative and qualitative requirements to maintain listing, including minimum stockholders' equity requirements. On September 1, 2017, we received a letter from the NYSE American stating that it had determined that we were not in compliance with Sections 1003(a)(iii) of the NYSE American Company Guide and the stockholders' equity continued listing standards applicable to us due to our recently reported stockholders' equity of \$3,734,756 as of June 30, 2017 and net losses in our five most recent fiscal years ended December 31, 2016. Prior to this, we were exempt from Section 1003(a) of the NYSE American Company Guide since our market capitalization was above \$50 million. We submitted a plan on October 2, 2017 advising the NYSE American of the actions that will be taken to regain compliance with the continued listing standards by March 19, 2019. On November 9, 2017, we received a letter from the NYSE American stating that the NYSE American had accepted our plan to regain compliance with the continued listing standards. On April 12, 2018, we received a letter from NYSE American stating that we are back in compliance with all the NYSE American continued listing standards set forth in Part 10 of the Guide, specifically Sections 1003(a)(ii) and (iii). Even though we are back in compliance with the NYSE American's listing standards, there can be no assurances that we will be able to continue to comply with the NYSE American's listing requirements.

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

Our management will have broad discretion as to the use of the net proceeds from any offering by us and could use them for purposes other than those contemplated at the time of this offering. Accordingly, you will be relying

S-16

Table of Contents

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.

The FDA is requiring an additional clinical trial of Ampion for OAK.

We have been engaged in discussions with the FDA relating to the nonclinical development and clinical evaluation of Ampion. Following our meeting with the FDA in July 2018, we received a response letter thereto. In the letter, the FDA stated that it considers the AP-003-A trial to be an adequate and well-controlled clinical trial that provides evidence of effectiveness of Ampion and can contribute to the substantial evidence of effectiveness necessary for approval of a BLA, but that as a single trial the AP-003-A study alone does not appear to provide sufficient evidence of effectiveness to support a BLA. The FDA did not consider the AP-003-C trial to be an adequate and well-controlled clinical trial and recommended that we perform an additional randomized trial with a concurrent control group and that we request a Special Protocol Assessment to obtain FDA concurrence of the trial design before beginning the study. We plan to continue to discuss the data and our BLA with the FDA and we cannot ensure the outcome of such subsequent discussions with the FDA. We also cannot ensure that the data derived from a subsequent trial will be sufficient to support a submission to the FDA of a BLA for Ampion. In the event that an additional clinical trial is necessary, we are evaluating the impact of such a trial on the potential timing for a submission of a BLA for Ampion and our expectations as to the cost of such a trial. We will also continue to address with the FDA the validation of manufacturing processes and controls and we cannot ensure when or whether we will receive validation.

Table of Contents

USE OF PROCEEDS

We estimate that the proceeds from this offering, after deducting estimated offering expenses payable by us and underwriting discounts and commissions, will be approximately \$ million. These amounts do 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 working capital and general corporate purposes, including continued preclinical development of Ampion and funding an Ampion clinical trial, if required. 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 from this offering in short-term, investment-grade, interest-bearing securities.

S-18

Table of Contents**DILUTION**

If you purchase shares of common stock and accompanying warrants in this offering, you will experience dilution to the extent of the difference between the public offering price of the shares of common stock in this offering (excluding shares of common stock issuable upon exercise of the warrants being offered in this offering) and the net tangible book value per share of our common stock immediately after this offering.

Our net tangible book value as of March 31, 2018 was approximately \$(8.9) million, or \$(0.103) 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 March 31, 2018.

After giving effect to the sale of _____ shares of common stock in this offering (excluding shares of common stock issuable upon exercise of the warrants being offered in this offering) at the public offering price of \$ _____ per share of common stock and warrant, and after deducting the underwriting discounts, commissions and estimated offering expenses payable by us, our as adjusted net tangible book value would have been approximately \$ _____ million, or approximately \$ _____ per share of common stock, as of March 31, 2018. This represents an immediate increase in net tangible book value of approximately \$ _____ per share to existing stockholders and an immediate dilution of approximately \$ _____ per share to new investors. The following table illustrates this calculation on a per share basis:

Public offering price per share	\$
Net tangible book value per share as of March 31, 2018	\$(0.103)
Increase in net tangible book value per share attributable to new investors	\$
As adjusted net tangible book value per share after giving effect to this offering	\$
Dilution per share to investors in this offering	\$

The number of shares of common stock shown above to be outstanding after this offering is based on 86,011,751 shares outstanding as of March 31, 2018 and excludes:

6,849,165 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2018, at a weighted average exercise price of \$2.81 per share;

3,042,262 shares of our common stock reserved for future issuance under our 2010 Stock Incentive Plan as of March 31, 2018;

7,647,744 shares of our common stock issuable upon the exercise of warrants outstanding as of March 31, 2018 (excluding the warrants offered hereby), at a weighted average exercise price of \$0.93 per share; and

_____ shares of common stock issuable upon exercise of warrants to be issued in this offering.

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 (excluding the warrants offered hereby). The exercise of outstanding options and warrants having an exercise price

less than the offering price will increase dilution to new investors. In addition, we may choose to raise additional capital depending on market conditions, our capital requirements and strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

S-19

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

Our common stock is traded on the NYSE American. The following table sets forth the intra-day high and low sale price information for our common stock as reported by the NYSE American for the periods indicated.

	High	Low
Year ending December 31, 2018		
1st Quarter	\$ 4.09	\$ 2.11
2nd Quarter	\$ 3.89	\$ 1.58
3rd Quarter (through August 7, 2018)	\$ 3.20	\$ 2.02
Year ended December 31, 2017		
1st Quarter	\$ 1.05	\$ 0.75
2nd Quarter	\$ 1.04	\$ 0.52
3rd Quarter	\$ 0.78	\$ 0.38
4th Quarter	\$ 4.95	\$ 0.61
Year ended December 31, 2016		
1st Quarter	\$ 3.50	\$ 1.69
2nd Quarter	\$ 4.32	\$ 0.84
3rd Quarter	\$ 1.45	\$ 0.70
4th Quarter	\$ 1.14	\$ 0.59

On August 7, 2018, the last reported sale price for our common stock on the NYSE American was \$2.86 per share. As of August 7, 2018, there were approximately 265 holders of record 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-21

Table of Contents

DESCRIPTION OF SECURITIES

In this offering, we are offering _____ shares of common stock and warrants to purchase up to _____ 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 authorized to issue 200,000,000 shares of common stock, par value \$0.0001 per share. As of March 31, 2018, there were 86,011,751 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 14 of the accompanying prospectus.

Warrants

The material terms and provisions of the warrants to purchase _____ 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 investors 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 _____ shares of common stock at an initial exercise price of \$ _____ per share. Each warrant may be exercised at any time beginning six months after the date of issuance and from time to time thereafter through and including the five-year anniversary of the initial exercise date.

Exercisability

The warrants will be exercisable commencing six months after the date of issuance and will expire on the five-year anniversary of the initial exercise date. 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

S-22

Table of Contents

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 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 number of shares of common stock issuable upon exercise of the warrants may be adjusted upon the occurrence of specific events, including 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, subject to certain conditions.

S-23

Table of Contents

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 the 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;

(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

S-24

Table of Contents

(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 of 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;

(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;

(iii) 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

CERTAIN U.S. FEDERAL INCOME TAX CONSIDERATIONS

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

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

a broker, dealer or trader in securities, currencies, commodities, or notional principal contracts;

a bank, financial institution or insurance company;

a regulated investment company, a real estate investment trust or grantor trust;

a tax-exempt entity or organization, including an individual retirement account or Roth IRA as defined in Section 408 or 408A of the Code, respectively;

a person holding the common stock or warrants as part of a hedging, integrated, or conversion transaction or a straddle, or a person deemed to sell common stock or warrants under the constructive sale provisions of the Code;

a trader in securities that has elected the mark-to-market method of tax accounting for securities;

an entity that is treated as a partnership or other pass-through entity for U.S. federal income tax purposes;

a person who is a partner or investor in a partnership or other pass-through entity that holds the common stock or warrants;

a U.S. person whose functional currency is not the U.S. dollar;

a controlled foreign corporation or passive foreign investment company;

a person who holds or receives common stock and warrants pursuant to the exercise of any employee stock option or otherwise as compensation;

a qualified foreign pension fund or an entity that is wholly owned by one or more qualified foreign pension funds; or

a U.S. expatriate and former citizens or long-term residents of the United States.

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

an individual who is a citizen or resident of the United States;

S-26

Table of Contents

a corporation (or any other entity treated as a corporation for U.S. federal income tax purposes) created or organized in or under the laws of the United States, any state thereof or the District of Columbia;

an estate the income of which is subject to U.S. federal income taxation regardless of its source; or

a trust if (1) it is subject to the primary supervision of a court within the United States and one or more U.S. persons have the authority to control all substantial decisions of the trust or (2) it has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

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

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

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

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

Investment Unit

The common stock and warrants should be treated for U.S. federal income tax purposes as an investment unit consisting of one share of our common stock and a warrant to purchase share of our common stock. For U.S. federal income tax purposes, the purchase price paid for each investment unit will be allocated between the shares of common stock and the warrants based on their respective relative fair market values. This allocation will be based upon our determination of the relative values of the warrants and of our common stock, which we will complete following the closing of the offering. While uncertain, the IRS, by analogy to the rules relating to the allocation of the purchase price to components of a unit consisting of debt and equity, may take the position that this allocation is binding on you unless you explicitly disclose in a statement attached to your timely filed U.S. federal income tax return for the tax year that includes your acquisition date of the unit that your allocation of the purchase price is different than our allocation. This allocation is not binding, however, on the IRS or the courts. Prospective investors are urged to consult their tax advisors regarding the U.S. federal income tax consequences of an investment in a unit, and the allocation of the purchase price paid for a unit.

Dividends on our Common Stock

We do not expect to declare or pay any distributions on our common stock in the foreseeable future. If we do make any distributions on shares of our common stock, however, such distributions will be includible in the gross income of

a U.S. holder as ordinary dividend income to the extent paid out of current or accumulated earnings and profits, as determined for U.S. federal income tax purposes. Any portion of a distribution in excess of current or accumulated earnings and profits would be treated as a return of the holder's tax basis in its common stock and then as gain from the sale or exchange of the common stock. Under current law, if certain requirements are met, a preferential U.S. federal income tax rate will apply to any dividends paid to a holder of common stock who is a U.S. individual.

S-27

Table of Contents

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

Sale of Common Stock or Warrants

A U.S. holder of common stock or warrants will generally recognize gain or loss on the taxable sale, exchange, or other taxable disposition of such stock or warrants in an amount equal to the difference between such U.S. holder's amount realized on the sale and its adjusted tax basis in the common stock or warrants sold. A U.S. holder's amount realized should equal the amount of cash and the fair market value of any property received in consideration of its stock or warrants. The gain or loss should be capital gain or loss and should be long-term capital gain or loss if the common stock or warrants are held for more than one year at the time of disposition. The deductibility of capital losses for U.S. federal income tax purposes is subject to limitations under the Code. Under current law, long-term capital gain recognized by an individual U.S. holder is generally eligible for a preferential U.S. federal income tax rate.

Exercise or Lapse of Warrants

Except as discussed below with respect to a cashless exercise of a warrant, upon the exercise of a warrant for common stock, a U.S. holder generally will not recognize gain or loss and will have a tax basis in the common stock received upon exercise equal to the U.S. holder's tax basis in the warrant, plus the exercise price of the warrant. The holding period for the common stock purchased pursuant to the exercise of a warrant will begin on the date following the date of exercise and will not include the period during which the U.S. holder held the warrant. If a warrant is allowed to lapse unexercised, a U.S. holder will recognize a capital loss in an amount equal to its tax basis in the warrant. Such loss will be long-term capital loss if the warrant has been held for more than one year as of the date the warrant lapsed. The deductibility of capital losses is subject to certain limitations.

The tax treatment of a cashless exercise of a warrant (i.e., where a portion of the holder's warrants are surrendered (the *Surrendered Warrants*) as the exercise price for other warrants to be exercised (the *Exercised Warrants*) as described above under *Description of Securities - Warrants*) is uncertain. Although the matter is not free from doubt, a cashless exercise should be treated as a tax-free transaction in which a holder's tax basis in the common stock received should equal the sum of the U.S. holder's tax basis in the *Surrendered Warrants* and the *Exercised Warrants*. It is also possible, however, that a cashless exercise could be treated as a taxable transaction, and a U.S. holder could recognize taxable gain or loss in an amount equal to the difference between the exercise price deemed paid and such U.S. holder's tax basis in the *Surrendered Warrants*. In this case, a U.S. holder's tax basis in the common stock received should equal the sum of the exercise price deemed paid and the U.S. holder's tax basis in the warrants exercised.

The holding period for common stock acquired in a cashless exercise will depend on the U.S. federal income tax treatment of a cashless exercise. The holding period for a share of common stock acquired in a cashless exercise would include the holding period of the *Surrendered Warrants* and *Exercised Warrants* if the cashless exercise is treated as a tax-free transaction. The holding period for a share of common stock acquired in a cashless exercise would begin on the day following the date of exercise if the cashless exercise is treated as a taxable exchange or treated similarly to a cash exercise (even if otherwise a tax-free transaction). Due to the absence of authority on the U.S. federal income tax treatment of a cashless exercise, there can be no assurance which, if any, of the alternative tax consequences and holding periods described above would be adopted by the IRS or a court of law. Accordingly, holders are urged to consult their tax advisors as to the tax consequences of a cashless exercise.

S-28

Table of Contents

Certain Adjustments to Warrants

Under Section 305 of the Code, an adjustment to the number of shares of common stock that will be issued on the exercise of the warrants, or an adjustment to the exercise price of the warrants, may be treated as a constructive distribution to a U.S. holder of the warrants if, and to the extent that, such adjustment has the effect of increasing such U.S. holder's proportionate interest in our earnings and profits or assets, depending on the circumstances of such adjustment (for example, if such adjustment is to compensate for a distribution of cash or other property to our shareholders). Adjustments to the exercise price of a warrant made pursuant to a bona fide reasonable adjustment formula that has the effect of preventing dilution of the interest of the holders of the warrants should generally not result in a constructive distribution. Any constructive distributions would generally be subject to the tax treatment described above under *Dividends on Our Common Stock*.

Information Reporting and Backup Withholding

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

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

Investment Unit

The common stock and warrants should be treated for U.S. federal income tax purposes as an investment unit consisting of one share of our common stock and a warrant to purchase _____ share of our common stock. For U.S. federal income tax purposes, the purchase price paid for each unit will be allocated between the shares of common stock and the warrants based on their respective relative fair market values.

Dividends on our Common Stock

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

on the holder's behalf, the holder will be required to provide appropriate documentation to the agent. The holder's agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. If a non-U.S. holder is eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty, such non-U.S. holder may obtain a refund or credit of any excess amounts withheld by filing an appropriate claim for a refund with the IRS in a timely manner.

S-29

Table of Contents

Dividends (including any dividends deemed to be received by you as described below under "Certain Adjustments to Warrants") received by a non-U.S. holder that are effectively connected with a U.S. trade or business conducted by the non-U.S. holder, or, if an income tax treaty between the United States and the non-U.S. holder's country of residence applies, are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder in the United States, are not subject to such withholding tax. To obtain this exemption, a non-U.S. holder must provide us or our paying agent with an IRS Form W-8ECI properly certifying such exemption. Such effectively connected dividends, although not subject to withholding tax, are taxed at the same graduated rates applicable to U.S. persons, as defined under the Code, net of certain deductions and credits, subject to any applicable income tax treaty providing otherwise. In addition to the graduated tax described above, dividends received by corporate non-U.S. holders that are effectively connected with a U.S. trade or business of the corporate non-U.S. holder may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty.

Sale of Common Stock or Warrants

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

the gain (1) is effectively connected with the conduct by the non-U.S. holder of a U.S. trade or business and (2) if an income tax treaty between the United States and the non-U.S. holder's country of residence applies, the gain is attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder in the United States, in which case the special rules described below apply;

the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of the sale, exchange or other disposition of our common stock, and certain other requirements are met, in which case the gain would be subject to a flat 30% tax, or such reduced rate as may be specified by an applicable income tax treaty, which may be offset by U. S. source capital losses, even though the individual is not considered a resident of the United States; or

if we are, or were within the shorter of the five-year period preceding the disposition and the non-U.S. holder's holding period, a U.S. real property holding corporation, or USRPHC.

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

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

Exercise or Lapse of Warrants

A non-U.S. holder will generally not be subject to U.S. federal income tax on any gains realized on the exercise of a warrant except as described above under Sale of Common Stock or Warrants . Except as discussed below with respect to a cashless exercise of a warrant, upon the exercise of a warrant, a non-U.S. holder generally will not recognize gain or loss upon exercise of a warrant.

S-30

Table of Contents

The tax treatment of a cashless exercise of a warrant (i.e., where a portion of the holder's warrants are surrendered (the *Surrendered Warrants*) as the exercise price for other warrants to be exercised (the *Exercised Warrants*) as described above under *Description of Securities*) is uncertain. Although the matter is not free from doubt, a cashless exercise should be treated as a tax-free transaction in which a holder's tax basis in the common stock received should equal the sum of the non-U.S. holder's tax basis in the *Surrendered Warrants* and the *Exercised Warrants*. It is also possible, however, that a cashless exercise could be treated as a taxable transaction, and a non-U.S. holder could recognize taxable gain or loss in an amount equal to the difference between the exercise price deemed paid and such non-U.S. holder's tax basis in the *Surrendered Warrants*. In this case, a non-U.S. holder's tax basis in the common stock received should equal the sum of the exercise price deemed paid and the non-U.S. holder's tax basis in the warrants exercised.

The holding period for common stock acquired in a cashless exercise will depend on the U.S. federal income tax treatment of a cashless exercise. The holding period for a share of common stock acquired in a cashless exercise would include the holding period of the *Surrendered Warrants* and *Exercised Warrants* if the cashless exercise is treated as a tax-free transaction. The holding period for a share of common stock acquired in a cashless exercise would begin on the day following the date of exercise if the cashless exercise is treated as a taxable exchange or treated similarly to a cash exercise (even if otherwise a tax-free transaction). Due to the absence of authority on the U.S. federal income tax treatment of a cashless exercise, there can be no assurance which, if any, of the alternative tax consequences and holding periods described above would be adopted by the IRS or a court of law. Accordingly, holders are urged to consult their tax advisors as to the tax consequences of a cashless exercise.

Certain Adjustments to Warrants

Under Section 305 of the Code, an adjustment to the number of ordinary shares that will be issued on the exercise of the warrants, or an adjustment to the exercise price of the warrants, may be treated as a constructive distribution to a non-U.S. holder of the warrants if, and to the extent that, such adjustment has the effect of increasing such non-U.S. holder's proportionate interest in our earnings and profits or assets, depending on the circumstances of such adjustment (for example, if such adjustment is to compensate for a distribution of cash or other property to our shareholders). Adjustments to the exercise price of a warrant made pursuant to a bona fide reasonable adjustment formula that has the effect of preventing dilution of the interest of the holders of the warrants should generally not result in a constructive distribution.

Information Reporting and Backup Withholding

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

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

the information reporting and backup withholding rules to them.

S-31

Table of Contents

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding on Foreign Accounts

Legislation known as the Foreign Account Tax Compliance Act and guidance issued thereunder (FATCA) imposes withholding taxes on certain types of payments made to foreign financial institutions and certain other foreign entities (including financial intermediaries). FATCA generally imposes withholding at a rate of 30% on payments to certain foreign entities of dividends (including deemed dividends on warrants) on our common stock and the gross proceeds of dispositions of our common stock or warrants, unless various U.S. information reporting and due diligence requirements (generally relating to ownership by U.S. persons of interests in or accounts with those entities) have been satisfied or the entity otherwise qualifies for an exemption. An intergovernmental agreement between the United States and an applicable foreign country may modify these requirements. These withholding rules generally apply to payments of dividends on common stock, and to payments of gross proceeds from a sale or other disposition of our common stock or warrants made on or after January 1, 2019. You should consult your tax advisor regarding the application of FATCA.

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

Table of Contents**UNDERWRITING**

We are offering the shares of common stock and accompanying warrants described in this prospectus supplement through the underwriter listed below. Subject to the terms and conditions set forth in the underwriting agreement between us and Canaccord Genuity LLC, as sole underwriter, we have agreed to sell to the underwriter, and the underwriter has severally agreed to purchase from us, the respective number of shares of common stock and accompanying warrants shown opposite its name below:

Name	Number of shares	Number of Shares Underlying Accompanying warrants
Canaccord Genuity LLC		
Total		

Subject to the terms and conditions set forth in the underwriting agreement, the underwriter has agreed to purchase all of the shares and accompanying warrants sold under the underwriting agreement if any of them are purchased.

We have agreed to indemnify the underwriter against certain liabilities, including liabilities under the Securities Act of 1933, as amended, and to contribute to payments the underwriter may be required to make for certain liabilities.

The underwriter is offering the shares and accompanying warrants, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by its counsel, including the validity of the shares and accompanying warrants, and other conditions contained in the underwriting agreement, such as the receipt by the underwriter of officer's certificates and legal opinions. The underwriter reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The underwriter has advised us that it proposes to offer the shares of common stock and accompanying warrants directly to the public at the public offering price set forth on the cover page of this prospectus supplement, and to dealers at the public offering price less a selling concession not in excess of \$ per share and accompanying warrant. The underwriter also may allow, and dealers may reallocate, a concession not in excess of \$ per share and accompanying warrants to brokers and dealers. After the public offering of the shares and accompanying warrants, the underwriter may change the offering price and other selling terms.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriter and the proceeds, before expenses, to us in connection with this offering (assuming none of the warrants issued in this offering are exercised).

Per Share and Accompanying	Total
---	--------------

	Warrant	
Public offering price	\$	\$
Underwriting discounts and commissions paid by us		
Proceeds, before expenses, to us	\$	\$

The expenses of the offering payable by us in connection with the offering, other than the underwriting discounts and commissions and the expense reimbursement referred to below, are estimated to be approximately \$. We are responsible for all of our expenses related to the offering, whether or not it is completed.

S-33

Table of Contents

In addition to the underwriting discounts and commissions to be paid by us, we have agreed to reimburse the underwriter for (i) up to \$75,000 of its out-of-pocket expenses incurred in connection with the offering, including travel, document production and distribution and database and research expenses and the reasonable fees and disbursements of counsel to the underwriter and (ii) the fees and disbursements of counsel to the underwriter in connection with FINRA matters in an amount not to exceed \$15,000 in the aggregate. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

Lock-Up Agreements

We have agreed that during a period of 150 days from the date of this prospectus supplement, we will not, without the prior written consent of Canaccord Genuity LLC, (i) directly or indirectly, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of any shares of our common stock or any securities convertible into or exercisable or exchangeable for shares of our common stock or file any registration statement under the Securities Act with respect to any of the foregoing or (ii) enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of shares of our common stock, whether any such swap or transaction described in clause (i) or (ii) above is to be settled by delivery of shares of common stock or such other securities, in cash or otherwise, subject to certain exceptions.

All of our executive officers and directors have agreed that they will not, without the prior written consent of Canaccord Genuity LLC, offer, sell, contract to sell, pledge or otherwise transfer or dispose of (or enter into any transaction which is designed to, or might reasonably be expected to, result in the disposition of (whether by actual disposition or effective economic disposition due to cash settlement or otherwise) by them or any of their affiliates or any person in privity with them or any of their affiliates), directly or indirectly, including the filing (or participation in the filing) of a registration statement with the SEC in respect of, or establish or increase a put equivalent position or liquidate or decrease a call equivalent position within the meaning of Section 16 of the Exchange Act, and the rules and regulations of the SEC promulgated thereunder with respect to, any shares of our common stock or any securities convertible into, or exercisable or exchangeable for our common stock, or publicly announce an intention to effect any such transaction, for a period from the date of this prospectus supplement until, and including the date that is, 90 days after the date of this prospectus supplement. Each of the lock-up agreements contains certain exceptions, including the establishment of a Rule 10b5-1 trading plan, provided that (i) such plan does not provide for the transfer of shares of common stock during the 90-day period and (ii) no public announcement or filing under the Exchange Act is required or voluntarily made regarding the establishment of such plan. This lock-up provision applies to shares of our common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition. Certain of our executive offices and directors may enter into Rule 10b5-1 trading plans.

Canaccord Genuity LLC may, in its sole discretion, release any of the securities subject to these lock-up agreements at any time without notice.

Price Stabilization, Short Positions and Penalty Bids

In connection with the offering, the underwriter may purchase and sell our common stock in the open market. These transactions may include stabilizing transactions, passive market making and purchases to cover syndicate short positions created in connection with the offering. Until distribution of the shares of our common stock is completed, SEC rules may limit the underwriter from bidding for and purchasing shares of our common stock. However, the underwriter may engage in transactions that stabilize the price of the shares of our common stock, such as bids or purchases to peg, fix or maintain that price. A stabilizing transaction is a bid for or the purchase of common stock on

behalf of an underwriter in the open market for the purpose of fixing or maintaining the price of the shares of common stock. Stabilizing transactions may cause the price of shares of our common stock to be higher than the price that might otherwise prevail in the open market.

S-34

Table of Contents

If an underwriter creates a short position in our common stock in connection with the offering (i.e., if it sells more shares of our common stock than are listed on the cover page of this prospectus supplement), the underwriter may reduce that short position by purchasing shares of our common stock in the open market. A covering transaction is the bid for or purchase of common stock on behalf of the underwriter to reduce a short position incurred by the underwriter in connection with the offering. A short position is more likely to be created if the underwriter is concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase shares in this offering. Similar to other purchase transactions, the underwriter's purchases to cover the short sales may have the effect of raising or maintaining the market price of our shares or preventing or retarding a decline in the market price of our shares. As a result, the price of our shares may be higher than the price that might otherwise prevail in the open market.

The underwriter may also impose a penalty bid, whereby the underwriter may reclaim selling concessions allowed to syndicate members or other broker-dealers in respect of the common stock sold in the offering for their account if the underwriter repurchases the shares in stabilizing or covering transactions. These activities may stabilize, maintain or otherwise affect the market price of the common stock, which may be higher than the price that might otherwise prevail in the open market. The imposition of a penalty bid may also affect the price of the shares of our common stock in that it discourages resales of those shares of our common stock.

In connection with the offering, the underwriters may also engage in passive market making transactions in our common stock on the NYSE American in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

The underwriter has advised us that these transactions may be effected on the NYSE American or otherwise. Neither we nor the underwriter make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of shares of our common stock. In addition, neither we nor the underwriter make any representation that the underwriter will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

This prospectus supplement and the accompanying prospectus may be made available in electronic format on websites or through other online services maintained by the underwriters of the offering, or by their affiliates. Other than this prospectus supplement and the accompanying prospectus in electronic format, the information on such websites and any information contained in any other website maintained by the underwriters or any of their affiliates is not part of this prospectus supplement, the accompanying prospectus or the registration statement of which this prospectus supplement and the accompanying prospectus form a part, has not been approved or endorsed by us or the underwriter in its capacities as an underwriter and should not be relied upon by investors.

Disclaimers About Non-U.S. Jurisdictions

United Kingdom

The underwriters:

have only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of section 21 of Financial Services and Markets Act 2000 (as amended) (FSMA)) to persons who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 or in circumstances in which section 21 of FSMA does not apply to us; and

S-35

Table of Contents

have complied with and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom.

Switzerland

The securities will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to article 652a or 1156 of the Swiss Federal Code of Obligations.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), an offer of our securities may not be made to the public in a Relevant Member State other than:

to any legal entity which is a qualified investor as defined in the Prospectus Directive;

to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the relevant dealer or dealers nominated by us for any such offer, or;

in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of our securities shall require us or the underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this description, the expression an offer of our securities to the public in relation to any of our securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the expression may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that member state, and the expression Prospectus Directive means European Union Directive 2003/71/EC (as amended by Directive 2010/73/EU) and includes any relevant implementing measure in each Relevant Member State.

Neither this prospectus supplement nor the accompanying prospectus is a prospectus for the purposes of the Prospectus Directive. This prospectus supplement and the accompanying prospectus have been prepared on the basis that any offer of our securities in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of securities. We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on our behalf, other than offers made by the underwriter and its respective affiliates, with a view to the final placement of the securities as contemplated in this document. Accordingly, no purchaser of the securities, other than the underwriter, is authorized to make any further offer of securities on our behalf or on behalf of the underwriter.

Canada

The securities may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

S-36

Table of Contents

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if the prospectus supplement or the prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriter is not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Relationship with Ampio Pharmaceuticals, Inc.

In the ordinary course of business, the underwriter and its affiliates in the future may provide various investment banking, financial advisory and other services to us for which they may receive customary compensation. In the course of their business, the underwriter and its affiliates may actively trade our securities for their own account or for the accounts of customers, and, accordingly the underwriter and its affiliates may at any time hold long or short positions in such securities.

Listing

Our common stock is listed on the NYSE American under the symbol AMPE. We do not intend to list the warrants on any national securities exchange or other trading market.

Transfer Agent

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

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. Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo P.C., Boston, Massachusetts, acted as counsel for the underwriter.

EXPERTS

The balance sheets of Ampio Pharmaceuticals, Inc. as at December 31, 2017 and 2016 and the related statements of operations, stockholders' equity and cash flows for each of the three years for the period ended December 31, 2017 and the related notes have been audited by EKS&H LLLP, independent registered public accounting firm, as stated in its report which is incorporated herein by reference from the Annual Report on Form 10-K for the fiscal year ended December 31, 2017. Such financial statements and schedule have been incorporated in reliance upon the report of such experts in accounting and auditing.

S-38

Table of Contents

PROSPECTUS

\$100,000,000

Common Stock

Preferred Stock

Debt Securities

Warrants

Units

**5,000,000 Shares of Common Stock Offered by
the Selling Stockholder**

Issuable Upon Exercise of Warrants

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

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

Each time we offer securities, we will provide the specific terms of the securities offered in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus

supplement and any related free writing prospectus, as well as any documents incorporated by reference, before buying any of the securities being offered.

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

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

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

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

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

The date of this prospectus is April 20, 2017.

Table of Contents

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	Page 1
<u>SUMMARY</u>	2
<u>RISK FACTORS</u>	5
<u>FORWARD-LOOKING STATEMENTS</u>	5
<u>RATIO OF EARNINGS TO COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS</u>	7
<u>USE OF PROCEEDS</u>	8
<u>SELLING STOCKHOLDERS</u>	9
<u>PLAN OF DISTRIBUTION</u>	11
<u>DESCRIPTION OF CAPITAL STOCK</u>	14
<u>DESCRIPTION OF DEBT SECURITIES</u>	19
<u>DESCRIPTION OF WARRANTS</u>	26
<u>DESCRIPTION OF UNITS</u>	27
<u>LEGAL MATTERS</u>	28
<u>EXPERTS</u>	28
<u>WHERE YOU CAN FIND ADDITIONAL INFORMATION</u>	28
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	28

Table of Contents

ABOUT THIS PROSPECTUS

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

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

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

Table of Contents

SUMMARY

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

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

Overview

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

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

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

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

Corporate Information

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

The Securities We May Offer

We may offer shares of our common stock, various series of preferred stock, debt securities and/or warrants to purchase our common stock, either individually or in units, with a total value of up to \$100,000,000 from time

Table of Contents

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

designation or classification;

aggregate principal amount or offering price;

maturity, if applicable;

original issue discount, if any;

rates and times of payment of interest or dividends, if any;

redemption, conversion, exchange or sinking fund terms, if any;

conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;

restrictive covenants, if any; and

voting or other rights, if any.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

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

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

the names of those agents or underwriters;

applicable fees, discounts and commissions to be paid to them;

details regarding over-allotment options, if any; and

the net proceeds to us.

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

Table of Contents

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

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of such series of preferred stock, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. We urge you to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into or exchangeable for our common stock or preferred stock. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

The debt securities will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. Forms of indentures have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered, will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

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

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

Table of Contents

Units. We may issue, in one or more series, units consisting of common stock and/or warrants for the purchase of common stock in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. In this prospectus, we have summarized certain general features of the units. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of units being offered, as well as the complete unit agreement, if any, that contains the terms of the units. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, any form of unit agreement and any supplemental agreements that describe the terms of the series of units we are offering before the issuance of the related series of units.

RISK FACTORS

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

FORWARD-LOOKING STATEMENTS

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

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

the results and timing of our clinical trials;

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

our manufacturing plans;

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

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

Table of Contents

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

the acceptance and approval of regulatory filings;

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

our plans to develop other product candidates; and

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

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

Table of Contents**RATIO OF EARNINGS TO COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS**

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

	Year Ended December 31, 2016	Year Ended December 31, 2015	Year Ended December 31, 2014	Year Ended December 31, 2013	Year Ended December 31, 2012
Ratio of earnings to combined fixed charges and preferred stock dividends	deficiency	deficiency	deficiency	deficiency	deficiency
Deficiency (in thousands)					
(\$)	\$ 19,163	\$ 32,010	\$ 38,125	\$ 24,009	\$ 11,593

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

Table of Contents

USE OF PROCEEDS

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

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

Table of Contents

SELLING STOCKHOLDER

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

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

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

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

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

The number of shares of common stock outstanding and percentage of beneficial ownership before this offering set forth below is computed on the basis of 57,242,164 shares of our common stock issued and

Table of Contents

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

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

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

* Less than one percent (1%).

- (1) Represents the number of shares of common stock that may be issued upon exercise of the warrants. For the purposes hereof, we assume the issuance of all such shares pursuant to a cash exercise. The actual number of shares of common stock issuable upon exercise of the warrants is subject to adjustment for any stock split, stock dividend or similar transaction involving the common stock, and could be materially less or more than such number depending on factors which cannot be predicted by us at this time. The actual number of shares of common stock described in this prospectus, and included in the registration statement of which this prospectus is a part, includes such additional number of shares of common stock as may be issued or issuable upon exercise of the warrants by reason of any stock split, stock dividend or similar transaction involving the common stock, in accordance with Rule 416 under the Securities Act.
- (2) The terms of the warrant held by the selling stockholder contains warrants prohibit any exercise that would cause such holder to hold in excess of 4.99% of our then issued and outstanding shares of common stock. This limitation may be increased to 9.99% of our then issued and outstanding shares of common stock upon 61 days prior written notice from CVI.
- (3) Assumes that the selling stockholder will sell all shares of common stock offered by it under this prospectus.

- (4) Consists of 5,000,000 shares of common stock issuable upon exercise of warrants. Heights Capital Management, Inc. is the investment manager to CVI Investments, Inc. and as such may exercise voting and dispositive power over these shares. The principal business address of CVI Investments, Inc. is P.O. Box 309GT, Ugland House, South Church Street, George Town, Grand Cayman, KY 1-1104, Cayman Islands.

Table of Contents

PLAN OF DISTRIBUTION

Ampio's Plan of Distribution

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

at a fixed price or prices, which may be changed;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

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

the name or names of the underwriters, if any;

the purchase price of the securities and the proceeds we will receive from the sale;

any over-allotment options under which underwriters may purchase additional securities;

any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;

any public offering price;

any discounts or concessions allowed or re-allowed or paid to dealers; and

any securities exchange or market on which the securities may be listed.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in

the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. Any public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. The prospectus supplement, naming the underwriter, will describe the nature of any such relationship.

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

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

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

Table of Contents

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

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or in the open market after the distribution is completed, to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters that are qualified market makers on the NYSE MKT LLC may engage in passive market making transactions in the common stock on the NYSE MKT LLC in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

Selling Stockholder's Plan of Distribution

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

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

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

in the over-the-counter market;

Table of Contents

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

through the writing or settlement of options or other hedging transactions, whether such options are listed on an options exchange or otherwise;

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

public or privately negotiated transactions;

through the settlement of short sales;

transactions in which broker-dealers agree with the selling stockholder to sell a specified number of such shares at a stipulated price per share;

a combination of any such methods of sale; or

any other method permitted pursuant to applicable law.

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

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

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

Table of Contents

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

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

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

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

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

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

DESCRIPTION OF CAPITAL STOCK

General

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

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

Common Stock

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

Table of Contents

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

Preferred Stock

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

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

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

the title and stated value;

the number of shares we are offering;

the liquidation preference per share;

the purchase price per share;

the dividend rate per share, dividend period and payment dates and method of calculation for dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

Table of Contents

our right, if any, to defer payment of dividends and the maximum length of any such deferral period;

the procedures for any auction and remarketing, if any;

the provisions for a sinking fund, if any;

the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock or other securities of ours, including depositary shares and warrants, and, if applicable, the conversion period, the conversion price, or how it will be calculated, and under what circumstances it may be adjusted;

whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange period, the exchange price, or how it will be calculated, and under what circumstances it may be adjusted;

voting rights, if any, of the preferred stock;

preemption rights, if any;

restrictions on transfer, sale or other assignment, if any;

whether interests in the preferred stock will be represented by depositary shares;

a discussion of any material or special United States federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

any limitations on issuances of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock being issued as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, rights, preferences, privileges, qualifications or restrictions of the preferred stock. The General Corporation Law of the State of Delaware, the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class (or, in some cases, as a series) on an amendment to our certificate of incorporation if the amendment would change the par value or, unless the certificate of incorporation provided otherwise, the number of authorized shares of the class or change the powers, preferences or special rights of the class or series so as to adversely affect the class or series, as the case may be. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

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

Delaware Anti-Takeover Law.

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

Table of Contents

interested stockholder is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock.

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

before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; or

upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) shares owned by:

persons who are directors and also officers; and

employee stock plans, in some instances; or

at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Staggered board of directors

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

Advance notice requirements for stockholder proposals and director nominations

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

Authorized but unissued shares

Our authorized but unissued shares of common stock and preferred stock are available for future issuances without stockholder approval and could be utilized for a variety of corporate purposes, including future offerings to raise additional capital, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could render more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Limitation on liability and indemnification of directors and officers

Our Delaware certificate of incorporation and bylaws provide that our directors and officers will be indemnified by us to the fullest extent authorized by Delaware law as it now exists or may in the future be

Table of Contents

amended, against all expenses and liabilities reasonably incurred in connection with their service for or on our behalf. Our bylaws permit us to secure insurance on behalf of any officer, director or employee for any liability arising out of his or her actions, regardless of whether Delaware law would permit indemnification.

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

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

Transfer Agent and Registrar

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

Table of Contents

DESCRIPTION OF DEBT SECURITIES

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

We will issue any senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue any subordinated debt securities under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement, of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The indentures will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We use the term trustee to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

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

General

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

the title;

the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;

any limit on the amount that may be issued;

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

the maturity date;

whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;

the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

Table of Contents

whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

the terms of the subordination of any series of subordinated debt;

the place where payments will be payable;

restrictions on transfer, sale or other assignment, if any;

our right, if any, to defer payment of interest and the maximum length of any such deferral period;

the date, if any, after which, the conditions upon which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;

the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option, to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;

whether the indenture will restrict our ability or the ability of our subsidiaries, if any at such time, to:

incur additional indebtedness;

issue additional securities;

create liens;

pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries;

redeem capital stock;

place restrictions on our subsidiaries' ability to pay dividends, make distributions or transfer assets;

make investments or other restricted payments;

sell or otherwise dispose of assets;

enter into sale-leaseback transactions;

engage in transactions with stockholders or affiliates;

issue or sell stock of our subsidiaries; or

effect a consolidation or merger;

whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;

a discussion of certain material or special United States federal income tax considerations applicable to the debt securities;

information describing any book-entry features;

provisions for a sinking fund purchase or other analogous fund, if any;

the applicability of the provisions in the indenture on discharge;

whether the debt securities are to be offered at a price such that they will be deemed to be offered at an original issue discount as defined in paragraph (a) of Section 1273 of the Internal Revenue Code of 1986, as amended;

the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;

Table of Contents

the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations or advisable in connection with the marketing of the debt securities.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement or free writing prospectus the terms on which a series of debt securities may be convertible into or exchangeable for our common stock, our preferred stock or other securities (including securities of a third-party). We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock, our preferred stock or other securities (including securities of a third-party) that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, the indentures will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible into or exchangeable for other securities of ours or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default Under the Indenture

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

if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended;

if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable at maturity, upon redemption or repurchase or otherwise, and the time for payment has not been extended;

if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and

if specified events of bankruptcy, insolvency or reorganization occur.

We will describe in each applicable prospectus supplement or free writing prospectus any additional events of default relating to the relevant series of debt securities.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal, premium, if any, and accrued interest, if any,

Table of Contents

due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the unpaid principal, premium, if any, and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity or security satisfactory to it against any loss, liability or expense. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

the direction so given by the holder is not in conflict with any law or the applicable indenture; and

subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

the holder has given written notice to the trustee of a continuing event of default with respect to that series;

the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the trustee or security satisfactory to it against any loss, liability or expense or to be incurred in compliance with instituting the proceeding as trustee; and

the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities, or other defaults that may be specified in the applicable prospectus supplement or free writing prospectus.

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

Modification of Indenture; Waiver

Subject to the terms of the indenture for any series of debt securities that we may issue, we and the trustee may change an indenture without the consent of any holders with respect to the following specific matters:

to fix any ambiguity, defect or inconsistency in the indenture;

to comply with the provisions described above under Consolidation, Merger or Sale;

to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act;

Table of Contents

to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;

to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under Description of Our Debt Securities General, to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

to evidence and provide for the acceptance of appointment hereunder by a successor trustee;

to provide for uncertificated debt securities and to make all appropriate changes for such purpose;

to add to our covenants such new covenants, restrictions, conditions or provisions for the benefit of the holders, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred to us in the indenture; or

to change anything that does not materially adversely affect the interests of any holder of debt securities of any series.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, subject to the terms of the indenture for any series of debt securities that we may issue or as otherwise provided in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

extending the stated maturity of the series of debt securities;

reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption or repurchase of any debt securities; or

reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that, subject to the terms of the indenture and any limitation otherwise provided in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

recover excess money held by the trustee;

compensate and indemnify the trustee; and

appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium and interest on, the debt securities of the series on the dates payments are due.

Table of Contents

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement or free writing prospectus, in denominations of \$1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement or free writing prospectus with respect to that series.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement or free writing prospectus, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement or free writing prospectus, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement or free writing prospectus the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series. If we elect to redeem the debt securities of any series, we will not be required to:

issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs.

Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

Table of Contents

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement or free writing prospectus any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Ranking of Debt Securities

The subordinated debt securities will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement or free writing prospectus. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

The senior debt securities will rank equally in right of payment to all our other senior unsecured debt. The senior indenture does not limit the amount of senior debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

Table of Contents

DESCRIPTION OF WARRANTS

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

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

General

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

the offering price and aggregate number of warrants offered;

the currency for which the warrants may be purchased;

if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;

if applicable, the date on and after which the warrants and the related securities will be separately transferable;

the number of shares of common stock purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;

the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;

the terms of any rights to redeem or call the warrants;

any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreements and warrants may be modified;

a discussion of any material or special United States federal income tax consequences of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

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.

Table of Contents

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

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

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Governing Law

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

Enforceability of Rights by Holders of Warrants

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

DESCRIPTION OF UNITS

We may issue, in one or more series, units consisting of common stock and/or warrants for the purchase of common stock in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The units may be issued under unit agreements to be entered into between us and a unit agent, as detailed in the prospectus supplement relating to the units being offered. The prospectus supplement will describe:

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

a description of the terms of any unit agreement governing the units;

a description of the provisions for the payment, settlement, transfer or exchange of the units; and

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

Table of Contents

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

LEGAL MATTERS

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

EXPERTS

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

WHERE YOU CAN FIND ADDITIONAL INFORMATION

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

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

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

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

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

Table of Contents

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

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

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

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

Table of Contents

Shares of Common Stock

Warrants to Purchase up to Shares of Common Stock

PROSPECTUS SUPPLEMENT

Canaccord Genuity

August , 2018