

Ampio Pharmaceuticals, Inc.
Form 424B5
August 08, 2018
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**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.

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ABOUT THIS PROSPECTUS SUPPLEMENT

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

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

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

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

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

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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.

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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

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein contain forward-looking statements within the meaning of Section 27A of the Securities Act, 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

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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.

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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

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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

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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

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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.

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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

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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.

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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.

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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;

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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.

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RISK FACTORS

*Investing in our securities involves a high degree of risk. In addition to the other information contained in this prospectus supplement and in the documents we incorporate by reference, you should carefully consider the risks discussed below and under the heading **Risk Factors** in our Annual Report on Form 10-K for the fiscal year ended December 31, 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.

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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

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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.

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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.

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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.

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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