Ampio Pharmaceuticals, Inc.
Form 424B5
September 26, 2013
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Filed pursuant to Rule 424(b)(5)
Registration No. 333-177116

PROSPECTUS SUPPLEMENT

(To Prospectus Dated October 28, 2011)

4,600,319 Shares

Ampio Pharmaceuticals, Inc.

Common Stock

$5.50 per share

Pursuant to this prospectus supplement and the accompanying prospectus, we are offering an aggregate of 4,600,319 shares of our common stock to a limited number of purchasers, mainly institutional investors (collectively, the Investors) pursuant to a securities purchase agreement we entered into with the Investors on September 25, 2013, at a price of $5.50 per share of common stock. The aggregate purchase price for the shares of common stock is approximately $25.3 million. We will receive net proceeds from the sale of these shares of approximately $24.8 million after deducting our estimated offering expenses.

We are not using any placement agent for this offering.

Our common stock is quoted on the NYSE MKT LLC, or NYSE MKT, under the symbol AMPE. The last reported sale price of our common stock on the NYSE MKT on September 25, 2013, was $6.61 per share.

Investing in our common stock involves risks. See Risk Factors beginning on page S-12 of this prospectus supplement.

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.

We currently anticipate that the closing of the offering will take place on or about September 30, 2013. On the closing date, we will issue the shares of common stock to the Investors and receive funds in the amount of the aggregate purchase price.

The date of this prospectus supplement is September 26, 2013

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus, gives more general information about securities we may offer from time to time, some of which does not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined together with all documents incorporated by reference. If the description of the offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information contained in this prospectus supplement. However, if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference into this prospectus supplement or the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement. You should not assume that the information appearing in this prospectus supplement, the accompanying prospectus, any related free writing prospectus or any document incorporated by reference is accurate as of any date other than the date of the applicable document. Our business, financial condition, results of operations and prospects may have changed since that date. You should rely only on the information contained in or incorporated by reference into this prospectus supplement or contained in or incorporated by reference into the accompanying prospectus to which we have referred you. We are responsible only for the information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus or information contained in a free writing prospectus that we authorize to be delivered to you. We have not authorized anyone to provide you with information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. The information contained in, or incorporated by reference into, this prospectus supplement and contained in, or incorporated by reference into, the accompanying prospectus is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of securities. This prospectus supplement and the accompanying prospectus may be used only for the purpose for which they have been prepared. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you under the captions Where You Can Find More Information and Incorporation of Certain Information by Reference in this prospectus supplement.

We are not making an offer to sell these securities in any jurisdiction where such an offer or sale is not permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the shares in certain jurisdictions or to certain persons within such jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about and observe any restrictions relating to the offering of the shares and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation. Neither this prospectus supplement nor the accompanying prospectus constitutes an offer, or an invitation on our behalf, to subscribe for and purchase any of the securities.

Unless otherwise mentioned or unless the context requires otherwise, throughout this prospectus supplement and any related free writing prospectus, the words Ampio Pharmaceuticals, Ampio, we, us, our, the company or similar references refer to Ampio Pharmaceuticals, Ir its subsidiaries on a consolidated basis. References to BioSciences in this prospectus supplement mean DMI BioSciences, Inc., now a wholly-owned subsidiary of ours. References to Life Sciences in this prospectus supplement mean DMI Life Sciences, Inc., which is our predecessor for accounting purposes and a wholly-owned subsidiary of ours. Life Sciences was

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formed in December 2008 and commenced operations when it acquired certain assets of BioSciences in April 2009. In March 2010, Life Sciences merged with a subsidiary of Chay Enterprises, Inc., a publicly traded Colorado corporation, which we refer to in this prospectus supplement as Chay Enterprises. Immediately after the merger, Chay Enterprises changed its name to Ampio Pharmaceuticals, Inc., and reincorporated in Delaware. We acquired BioSciences, now a wholly-owned subsidiary of ours, in March 2011. References to Luoxis in this prospectus supplement mean Luoxis Diagnostics, Inc., which is an 80.9% owned subsidiary of ours and was formed on January 24, 2013 to focus on the development and commercialization of the Oxidation Reduction Potential (ORP) technology platform.

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

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

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

- our expectations related to the use of proceeds, if any, from this offering;
- our need for, and ability to raise, additional capital;
- the results and timing of our clinical trials;
- the regulatory review process and any regulatory approvals that may be issued or denied by the Food and Drug Administration (FDA), the European Medicines Agency (EMA), or other regulatory agencies;
- our 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;

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- 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 supplement entitled Risk Factors, which we believe over time, could cause our actual results, performance or achievements to differ from the anticipated results, performance or achievements that are expressed or implied by our forward-looking statements. We have no duty to, and do not intend to, update or revise the forward-looking statements in this prospectus 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 supplement entitled Where You Can Find More Information and Incorporation of Certain Information by Reference and the sections of the accompanying prospectus 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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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in, or incorporated by reference into, this prospectus supplement. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, you should read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference in this prospectus supplement and the accompanying prospectus. If you invest in our common stock, you are assuming a high degree of risk. See Risk Factors in this prospectus supplement beginning on page S-12. All references in this prospectus supplement to our consolidated financial statements include, unless the context indicates otherwise, the related notes.

Company Overview

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

Background

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

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

Business Overview

Our Product Pipeline

Ampion for Osteoarthritis and Other Inflammatory Conditions

Ampion is a sub 5000 molecular weight (MW) fraction of commercial human serum albumin (HSA). The primary constituent ingredient is aspartyl-alanyl diketopiperazine, or DA-DKP, an endogenous immunomodulatory molecule derived from the N-terminus of HSA. Based on Ampio s published in-vitro findings, DA-DKP appears to play a significant role in the homeostasis of inflammation. DA-DKP is believed to reduce inflammation by suppressing pro-inflammatory cytokine production in T-cells. Ampion also contains other known small molecules that confer anti-inflammatory effects to complement the activity of DA-DKP and derive in-vitro and in-vivo effects. We believe the non-steroidal, low molecular weight, anti-inflammatory biologic has the potential to be used in a wide variety of acute and chronic inflammatory conditions as well as immune-mediated diseases. Ampio is currently developing Ampion as an intra-articular injection to treat osteoarthritis of the knee.

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Ampion is manufactured as the low molecular weight filtration product of commercial human serum albumin containing DA-DKP, N-acetyltryptophan, caprylate, and other small molecules either contained in HSA or added to HSA during the processing and production of commercial HSA products. DA-DKP, the primary constituent ingredient contained in Ampion, is a locally generated molecule formed as a physiological result of the cleavage and cyclization of the N-terminal aspartic acid and alanine residues of human albumin. The molecule was originally discovered in the blood and cerebrospinal fluid of patients several days after suffering severe closed head injuries. A high concentration of DA-DKP has also been detected in biofilms found on endotracheal tubes recovered from intubated patients and on implanted orthopedic plates and screws. Together these findings suggest a mechanism by which DA-DKP contributes to the ability to reduce the body s inflammatory response following insult or injury.

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

Market Opportunity.

Osteoarthritis is the most common form of arthritis, affecting over 27 million people in the United States. It is a progressive disorder of the joints involving degradation of the intra-articular cartilage, joint lining, ligaments, and bone. The incidence of developing osteoarthritis of the knee or hip over a lifetime is approximately 45% and 25%, respectively. 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 therapeutics market continues to expand and is expected to exceed $7 billion by 2015 and the global demand for osteoarthritis of the knee treatment is expected to be fueled by favorable demographics and increasing awareness of treatment options. Despite the size and growth of the osteoarthritis of the knee market, few adequate treatment options currently exist.

Inflammation of the synovium interrupts the natural chondrocyte metabolism, which is responsible for the production and maintenance of the components of cartilage s extracellular matrix. Osteoarthritic synovial fluid activates pro-inflammatory cytokines in active chondrocytes through autocrine and paracrine mechanisms. The cytokines, such as tumor necrosis factor-a (TNF-a), interleukin-17 (IL-17), and interleukin-18 (IL-18), stimulate the synthesis of matrix metalloproteinase (MMPs) whose enzymatic activity leads to the digestion of cartilage.

Phase I Clinical Trial Results.

In October 2011, we announced results from the first part of our Ampion-in-Knee (AIK) study of Ampion in the treatment of osteoarthritis of the knee. We conducted our Phase I trial in Australia because the biologics legislation governing the Australian Therapeutic Goods Administration (TGA) allowed us to move Ampion directly into human clinical trials as the TGA recognized that HSA has an already established safety profile in humans by virtue of its longstanding commercial use. The AIK trial was conducted in patients diagnosed with moderately-severe to severe osteoarthritis of the knee. The 60 patients were enrolled in a 3 arm randomized double-blind trial designed to establish tolerability and efficacy of Ampion. In the three arms of the trial, patients were injected in the knee with: (i) steroid, lidocaine, and saline; (ii) steroid, lidocaine, and Ampion, and; (iii) steroid, saline, and Ampion. There were very few moderate to severe adverse events with those subjects receiving the standard of care (Lidocaine/Steroids, 3 patients or 15%) and even fewer in either arm receiving

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Ampion in addition to steroids (2 patients or 10%). Overall, there were 4 treatment-related adverse events reported, but no moderate to severe treatment-related adverse events were reported. Upon establishing Ampion was safe for human use, these favorable results allowed us to proceed to the second part of the Phase I trial evaluating Ampion as a monotherapy against saline.

In April 2012, we announced results from the second part of our AIK study of Ampion in the treatment of osteoarthritis of the knee. The second part of the AIK study was a 30 patient randomized (1:1), double-blind, vehicle controlled trial designed to evaluate the safety and efficacy of Ampion 4mL in osteoarthritis of the knee patients. The 30 patients represented the efficacy evaluable population who did not receive a betamethasone injection as rescue medication of the intent-to-treat population of 43 patients. The primary endpoint was mean change in pain from baseline for Ampion compared to saline at 84 days following a single intra-articular injection into the knee measured on the pain scale known as the Numerical Rating Scale (NRS). Secondary endpoints included evaluating the safety as well as rescue medication use (acetaminophen), and responder rate (defined as a 2 point reduction in pain on the NRS). A brief summary of the combined Ampion topline results is as follows:

- Patients receiving Ampion achieved a significantly greater reduction in pain from baseline to 12 weeks compared to saline vehicle control (1.76; p=0.04).

- Patients receiving Ampion achieved a greater responder rate, defined as a 2 point shift on the NRS, from baseline to 12 weeks compared to saline vehicle control (63% vs. 33%; p=0.10).

Overall, patients receiving Ampion achieved a statistically significant -2.22 reduction in pain from baseline ($p<0.05$) to 12 weeks compared to saline vehicle control (-0.46; p=0.34). A graph depicting the least squares (LS) mean change in pain from baseline for both Ampion and saline vehicle control is depicted below.

Clinical Development Pathway.

Upon conclusion of the AIK trial which yielded the positive results summarized above, we presented a package containing both pre-clinical and clinical data to the blood products division of the Center for Biologics Evaluation and Research (CBER) of the FDA. The original guidance toward an Ampion Biologics License Application (BLA) filing included instruction to conduct customary toxicology work inclusive of animal studies prior to progressing into U.S. human trials. However, following the FDA s recognition of the established safety

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profile and standardization of production of HSA, the FDA allowed us to progress directly into U.S. human clinical trials. The FDA initially indicated that we should design and conduct two well-controlled trials with a 12 week primary endpoint measured on the Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain subscale (WOMAC A). If we wished to request a chronic use label for Ampion, we would need to expose 1,500 patients to Ampion, including exposure of 300-600 patients for at least six months and 100 patients for at least one year, according to the FDA s ICH-E1A guidance.

In February 2013, in response to our Investigational New Drug (IND) application and two submissions describing two concurrent Phase III study protocols enrolling in excess of 1,600 patients, the FDA did not object to two sequential well-conducted trials in support of a license application. Under such a development program the dose ranging trial objectives would be twofold: compare two volumes for efficacy and safety and demonstrate statistical power. We referred to the dose ranging trial as our SPRING study.

Dose Ranging SPRING Trial Results.

On August 14, 2013, we announced results of the SPRING study of Ampion for the treatment of osteoarthritis of the knee. The SPRING study was a U.S. multicenter randomized (1:1:1:1), double-blind, vehicle controlled trial designed to evaluate the safety and efficacy of Ampion in osteoarthritis of the knee patients. 329 patients were randomized to receive one of two doses (4 mL or 10 mL) of Ampion or corresponding saline control via intra-articular injection. The primary study objective was to evaluate the relative efficacy of Ampion 4 mL versus Ampion 10 mL. The primary endpoint was mean change in pain as measured on the WOMAC, a standardized scoring metric for pain, from baseline for Ampion compared to the same volume of saline. Secondary endpoints included evaluating safety and quality of life, as well as stiffness and function. Ampion dose cohorts experienced statistically significant reductions in pain compared to control. There were no significant differences between the efficacy of the two Ampion doses. Selection of the optimal dose for the Phase III pivotal trial will be decided in consultation with the FDA. A brief summary of the combined Ampion topline results is as follows:

- Patients receiving Ampion achieved significantly greater reduction in pain (WOMAC A) from baseline to 12 weeks compared to saline vehicle control ($p = 0.0038$).
- Patients receiving Ampion experienced, on average, a greater than 40% reduction in pain from baseline.
- Patients receiving Ampion also achieved significantly greater improvement in function (WOMAC C) from baseline to 12 weeks compared to saline vehicle control ($p = 0.044$).
- Patients receiving Ampion also demonstrated significantly greater improvement in overall quality of life measures (Patient Global Assessment) from baseline to 12 weeks compared to saline vehicle control ($p = 0.012$).
- Clinical efficacy defined as pain reduction was evident as early as four weeks after the injection ($p = 0.025$) and continued to show improvement through 12 weeks ($p = 0.0038$).
- Ampion was well tolerated with minimal adverse events (AEs) reported in the study. AEs were well balanced between Ampion and control groups. There were no drug-related serious adverse events (SAEs).

Future Development.

We expect to share the SPRING trial data with the FDA prior to and during the October 29, 2013 Pre-BLA meeting scheduled by the FDA and start the Phase III pivotal trial based upon these discussions. We currently expect that the upcoming Phase III pivotal trial will be a U.S. multicenter, randomized (1:1) double-blind, vehicle controlled trial enrolling approximately 500 patients evaluating the difference in reduction in pain of Ampion 4 mL to a saline vehicle comparator of identical injection volume. We currently expect to commence enrollment in the Phase III pivotal trial in fourth quarter of 2013, announce top-line results in the second quarter of 2014. We

believe that the number of patients enrolled in our dose ranging SPRING trial and the number of patients planned for enrollment in the Phase III pivotal trial will meet the safety requirements of the FDA, and that these two trials will fulfill the clinical study requirements allowing us to proceed to a BLA filing for Ampion for treatment of osteoarthritis of the knee in the third quarter of 2014.

We plan to use a portion of the proceeds of this offering to design, develop and scale up a manufacturing facility where we would manufacture Ampion for registration batching and commercial supply as well as future clinical supplies. We have identified multiple potential production facilities in the Denver, CO metro area and have drafted proposed scale up plans. We have also initiated preliminary discussions regarding HSA raw material supply agreements with manufacturers.

We also plan to initiate market development activities for Ampion, including engagement of thought leaders as well as development of pricing, reimbursement, and coding strategy to maximize Ampion s value proposition. This market development work will maximize commercial possibilities as we progress toward the submission of the Ampion BLA.

We also intend to study Ampion for therapeutic applications outside of osteoarthritis of the knee. We expect to engage development partners to study Ampion in various conditions including: (i) acute and chronic inflammatory conditions; (ii) degenerative bone diseases; and (iii) respiratory and allergic disorders. Based on the continuing evaluation, we are also studying Ampion s effects on cellular behavior to indicate potential effects on disease modification across multiple conditions. If successful, we believe these additional formulations and potential therapeutic indications will supplement the Ampion clinical portfolio, and will enable clinical applications in large therapeutic markets where there are significant unmet needs. We expect that initial investigations into strategically attractive indications will be conducted on an investigator-sponsored basis.

Competition.

The currently available treatments for osteoarthritis of the knee include oral non-steroidal anti-inflammatory agents, opioids, pain patches, intra-articular (IA) corticosteroids, and hyaluronic acid (HA) injections. Despite wide availability and years of clinical use, none of these agents are recommended for use as evidenced by the most recently published knee osteoarthritis clinical practice guidelines. In May 2013, the American Academy of Orthopedic Surgeons (AAOS) issued their second edition of clinical practice guidelines for the treatment of osteoarthritis of the knee. The AAOS was unable to recommend for or against the use of intra-articular corticosteroid injections as studies designed to indicate efficacy are inconclusive. Further, the AAOS was also unable to recommend for or against the use of acetaminophen, opioids, or pain patches as the efficacy studies in this area are also inconclusive. Most importantly, the AAOS does not recommend (with a strong strength of recommendation) the use of hyaluronic acid injections as, in the association s assessment, the clinical evidence does not support their use. This latest clinical practice guideline underscores a pervasive unmet need in the treatment of osteoarthritis of the knee given few accepted and available treatments. We believe Ampion is a novel treatment option that, if approved, would be the first non-steroidal, non-hyaluronic-based intra-articular treatment available for the treatment of osteoarthritis of the knee.

Intellectual Property and Data Exclusivity.

As of September 1, 2013, the current Ampion patent portfolio consists of 44 issued patents and 42 pending applications worldwide. The portfolio primarily consists of two families filed in the United States and throughout the world. The first family includes four issued U.S. patents and one issued European Patent Office (EPO) patent validated in 19 countries with claims relating to methods of treating inflammatory disease and compositions of matter comprising diketopiperazine derivatives, including DA-DKP. This family also includes issued patents in Canada, China, Hong Kong, Japan and South Africa and two pending applications in the U.S. The standard 20-year expiration for patents in this family is

in 2021.

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The second family includes four issued U.S. patents with claims directed to methods of treating inflammation and T-cell mediated or inflammatory diseases with compositions of matter comprising DA-DKP. This family also includes issued patents in Australia, India, New Zealand, Singapore and South Africa and pending applications in the U.S., Australia, Canada, China, EPO, Israel, Japan and Korea. The standard 20-year expiration for patents in this family is in 2024.

In addition, as provided by the Patient Protection and Affordable Care Act (PPACA), the FDA will grant newly approved biologic agents 12 years of data exclusivity. We believe Ampion, if approved, would qualify for such exclusivity.

Optina for Diabetic Macular Edema

Optina is a low-dose formulation of danazol that we are developing to treat diabetic macular edema. 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 (cAMP) through the rapid activation of membrane-associated androgen, steroid binding globulin, and calcium channel receptors. At lower concentrations such as Optina, danazol binds to androgen and steroid binding globulin receptors stimulating the formation of a cortical actin ring. At higher concentrations, activation of the calcium channels shift the balance towards stress fiber formation and increase vascular permeability.

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

Market Opportunity.

Type 1 and type 2 diabetes mellitus affects 26 million people in the United States. One of the many symptoms of diabetes is the local and systemic inflammation of the microvascular system. Diabetic retinopathy is a complication of diabetes and is characterized by damage to the blood vessels of the retina and can either be proliferative or non-proliferative. Proliferative damage occurs when a reduction in oxygen levels in the retina due to impaired glucose metabolism causes fragile blood vessels to grow in the vitreous humor. Non-proliferative damage occurs when existing vessels experience poor endothelial cell linkage due to increased blood glucose levels and hypertension. Macular edema is the most common form of non-proliferative diabetic retinopathy. In diabetic macular edema, prolonged hyperglycemia compromises endothelial cell linkage leading to vascular permeability. The leakage of fluid, solutes, proteins and immune cells cause the macula to swell and thicken. This leads to damage of the central retinal tissue and can significantly impair sharp central vision. The prevalence of diabetes is 11.3% of the population above the age of 20, with an annual incidence of 1.9 million cases in the United States alone. In this population, the prevalence of diabetic macular edema is estimated at 30% of patients inflicted by the disease for 20 years or more.

Phase II results.

In 2012, we concluded our Phase II randomized, double-masked, placebo-controlled, dose-ranging study evaluating the efficacy and safety of Optina in subjects with diabetic macular edema at St. Michael s Hospital in Toronto, Canada. The trial was randomized (1:1:1:1) and included 34 patients with moderate to severe diabetic macular edema (316-707 microns of central retinal thickness) that were treated orally with either one of three

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doses of Optina (5mg, 15mg, 45mg) twice a day (BID) or placebo for 12 weeks. The primary endpoint was mean central retinal thickness (CRT) measured by optical coherence tomography (OCT). Secondary endpoints included improvement in best corrected visual acuity (BCVA) and safety. On a pooled basis, Optina failed to demonstrate significant reduction in CRT versus placebo.

The trial was terminated early based on the review of the interim analysis data. No significant safety issues were identified, but the overall study design was complicated by the lipophilic nature of danazol. That lipophilic nature when combined with the critical nature of the blood level (as compared to tissue level) meant that the dose administered to all the patients needed to take Body Mass Index (BMI) into account. Patients who were randomly allocated to a dose not appropriate for their body mass did not contribute scientifically useful proof of efficacy (or lack thereof). We, therefore, decided to terminate this study and initiate a redesigned study to evaluate the safety and efficacy of danazol dosing based on BMI.

However, recognizing danazol is very fat soluble, we subsequently stratified patients by body mass index (BMI). These results produced a strong correlation between BMI and efficacy at the different doses of Optina. A brief summary of the topline results is as follows:

- Patients stratified around a BMI of 35 receiving Optina 15mg BID achieved significant reduction in CRT (96.24 microns; p=0.01).
- Patients stratified around a BMI of 26 receiving Optina 5mg BID achieved a trend toward significant reduction in CRT (166.08 microns; p=0.13).
- 47% of patients receiving Optina improved at least one BCVA category.
- Two serious adverse events were identified, one unlikely related and one unrelated to Optina. There were three treatment related adverse events (TRAEs) all of which were considered possibly related to Optina.

Overall, patients receiving Optina achieved a reduction in CRT in a BMI dosage-adjusted manner at 12 weeks in the per-protocol population (n=23).

Clinical Development Pathway.

Danazol has been on the market for more than three decades with approved dosing of 200mg to 800mg. There also exist peer-reviewed publications studying the safety and efficacy in lower doses for the approved

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indications, such as idiopathic thrombocytopenic purpura. Given the vast body of safety data, we leveraged the established drug profile and are pursuing approval of Optina under the §505(b)(2) regulatory pathway, referencing the preexisting danazol literature. The FDA indicated that this approach to approval of Optina is acceptable after we presented results from the Phase II trial to the ophthalmology division of the Center for Drug Evaluation and Research (CDER) of the FDA. Under this clinical pathway, we confirmed with the ophthalmology division of the CDER that it may be possible for Optina to be approved on the basis of positive results from a single clinical trial accompanied by additional literature, such as an existing Drug Master File (DMF), toxicology work, and contra-indications, which would allow us to proceed to a New Drug Application (NDA) filing.

Clinical Trials in Support of a §505(b)(2) NDA.

The FDA has indicated that, for §505(b)(2) NDAs, complete studies of the safety and effectiveness of a candidate product may not be necessary if appropriate bridging studies provide an adequate basis for reliance upon FDA s findings of safety and effectiveness for a previously approved product. In support of a §505(b)(2) application for Optina, we commenced enrollment in a 450 patient Phase IIb trial in February 2013. The U.S. multicenter dose ranging trial is designed to evaluate the safety and efficacy of oral Optina compared with placebo over 12 weeks in adult patients with DME. The active treatment duration of 12 weeks is the maximum time allowed to withdraw treatment in the ophthalmology community. We have enrolled over 200 patients and expect enrollment to be completed in the first quarter of 2014. Patients are randomized (1:1:1) to receive one of two oral doses of Optina (0.5mg per BMI and 1.0mg per BMI per day) or placebo. The primary endpoint is improvement in best-corrected visual acuity in treated patients compared to a placebo. Secondary endpoints are (i) measurements of changes in central macular thickness in treated patients compared to a placebo and (ii) safety and tolerability of the two Optina doses. We anticipate releasing top-line results in the third quarter of 2014.

Additionally, patients from the active treatment arms of the trial will be followed for four weeks without treatment following the 12 week treatment period in order to study any regression of effect. All patients will also be given the option to enter into an open label extension of the trial. The open label study will evaluate patients improvement in BCVA over 12 weeks by administering the optimal dose of Optina. The optimal dose will be one of the two studied in the trial determined by an interim analysis occurring at week 4 involving approximately 150 patients. We expect to make an announcement around the interim analysis in the fourth quarter of 2014.

Future Development.

While we believe the data from a single clinical trial would support a NDA filing, we will assess the need for an additional trial in conjunction with the FDA upon the successful outcome of the trial in support of a §505(b)(2) NDA. The FDA has previously indicated that a Phase III trial may be necessary following the current trial. During this current trial, we are also gathering data on patients proteinuria levels. If Optina proves to be successful in inhibiting vascular permeability, we will assess the prospects of Optina for treatment of other diabetic angiopathies such as diabetic nephropathy.

Competition.

There is no orally administered treatment for DME currently available nor one to our knowledge being tested in clinical trials. The current standard of care in the U.S. for the treatment of DME is laser photocoagulation. The first and only approved therapy in the U.S. is intravitreal Lucentis (ranibizumab) injections. Ranibizumab belongs to a therapeutic class inhibiting vascular endothelial growth factor agonist (anti-VEGF). It is important to note, there is significant competition from off-label anti-VEGF treatment of DME from bevacizumab. Iluvien, fluocinolone acetonide micro-insert intravitreous implant, is available in six European countries, and is awaiting FDA marketing approval in

patients suffering from DME with a Prescription Drug User Fee Act (PDUFA) goal date of October 17, 2013. Ozurdex (dexamethasone intravitreal implant) is available in the U.S. for macular edema following retinal vein occlusion and noninfectious uveitis and the product s

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sponsor has submitted for U.S. and European approval in DME. Recently, two positive one-year results were announced from two Phase III trials of bimonthly intravitreal Eylea (aflibercept) injections (after five initial monthly injections), and the product s sponsor plans marketing regulatory submissions in DME by the end of 2013. Aflibercept is also an anti-VEGF antibody.

Intellectual Property.

As of September 1, 2013, the Optina patent portfolio currently consists of 40 issued patents and 44 pending applications worldwide. The portfolio consists primarily of one patent family which includes one issued patent in each of the U.S., EPO (validated in 36 countries) and Canada with claims relating to methods of treating macular edema with danazol. This family also includes pending applications in Australia, Brazil, China, Eurasian Patent Organization, Indonesia, Israel, Japan, Korea, Mexico, Malaysia, New Zealand, Philippines, Singapore, and South Africa. The standard 20-year expiration for patents in this family is in 2030.

Other Products

Sexual Dysfunction Portfolio

Zertane is an on-demand, orally dissolving tablet under development for the treatment of premature ejaculation, a condition that has a major impact on the quality of life for men and their sexual partners. The active ingredient, tramadol, has multiple mechanisms that can delay ejaculation. This drug also has an excellent safety record established during 30 years of human use for other medical indications. Zertane-ED, a combination of Zertane and a PDE-5 inhibitor, can be used to treat premature ejaculation and erectile dysfunction. Ampio is actively seeking a partnership for the completion of the U.S. Phase III clinical trials and worldwide commercialization of Zertane. In June 2013, Ampio submitted the application to the Therapeutic Goods Administration (TGA) for approval of Zertane in Australia. We expect to receive approval for marketing Zertane in Australia in 2014.

Luoxis Diagnostics

In January 2013, we formed a subsidiary, Luoxis Diagnostics, which is an in-vitro diagnostics company focused on the development and commercialization of our ORP technology platform. All of the technology and patents related to the ORP technology platform as well as other diagnostic technologies have been assigned to Luoxis. Our novel ORP diagnostic platform is comprised of a point of care device and disposable testing strips that together measure the presence of oxidative stress and antioxidant reserves in patients. These measures can be applied across multiple acute illnesses and injuries as well as chronic diseases. Ampio owns 80.9% of Luoxis, and the balance is owned by non-affiliated investors.

Our ORP Diagnostic System is the only in-vitro diagnostic test that measures human ORP, an important, complete measure of oxidative stress that is implicated in both critical and chronic illnesses. As demonstrated over decades in multiple peer-reviewed publications, ORP is an important marker in the assessment of patient morbidity across a wide range of diseases and conditions. There are numerous clinical applications for this oxidative stress marker for which there is no currently available diagnostic test. Knowing the antioxidant reserves and ORP status of a patient is important for clinical management of the patient in the hospital or for discharge disposition and adds an objective metric for resuscitation efforts on a real-time basis from a single drop of plasma.

In June 2013, Luoxis announced positive Phase III summary data using our ORP Diagnostic System. The results are reported from a cohort of 153 elderly patients who suffered hip fractures as a result of a fall, the most common cause of hip fractures among the elderly. This study was performed by Luoxis using stored plasma samples of patients that were prospectively collected from patients diagnosed with a fall-related hip fracture. The study was conducted at a single site in the U.S. When studying the markers measured by the ORP diagnostic

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system, investigators demonstrated statistically significant correlations between patients antioxidant reserve levels and established comorbidity measures as measured by the Charlson Comorbidity Index (p=0.02). Investigators also reported a statistically significant correlation between patients ORP levels and injury severity as measured by the validated Injury Severity Score (ISS; p=0.01). These clinical study results indicate the predictive value of oxidation-reduction potential and antioxidant reserves and their value as prognostic markers among elderly hip fracture patients in a clinical setting. Hip fracture in patients over 65 years of age is associated with 2-3% in hospital mortality and grows to approximately 20-30% in the following six months.

NCE 001

NCE001 (para-phenoxy-methylphenidate) is a novel, small molecule methylphenidate derivative. Its basic mechanism of action is believed to be to increase methylation of the catalytic sub unit of Protein Phosphatase 2 A (PP2A), with activation of this phosphatase achieving an effect similar to kinase inhibitors. PP2A is known to be largely involved in inflammation, angiogenesis, and cell proliferation, and by decreasing phosphorylation, the intracellular phosphatase inhibits pro-carcinogenic cytokines and chemokines and cell signaling factors. Our pre-clinical research is focused on neuroblastoma, glioblastoma multiforme, renal cell carcinoma, and inflammatory breast cancer.

Company Information

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

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

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

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

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

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

Our principal executive offices are located at 5445 DTC Parkway, Suite 925, Greenwood Village, Colorado 80111, and our telephone number is (720) 437-6500. Additional information about us is available on our website at www.ampiopharma.com. The information contained on or that may be obtained from our website is not, and shall not be deemed to be, a part of this prospectus.

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The Offering

Common Stock Offered By Us	4,600,319 shares
Common Stock To Be Outstanding Immediately After This Offering	41,731,258 shares
NYSE MKT Listing Symbol	Our common stock is listed on the NYSE MKT under the symbol AMPE.
Use Of Proceeds	We estimate that our net proceeds from this offering, after deducting our estimated offering expenses, will be approximately $24.8 million based upon a price of $5.50 per share. We anticipate that we will use the net proceeds from this offering for working capital and for general corporate purposes, including continuation and completion of our Ampion and Optina clinical trials, potential submission of a BLA relating to Ampion and a NDA relating to Optina, acquisition of manufacturing equipment and related outfitting in connection with the leasing of a new manufacturing facility and the potential hiring of additional personnel to manufacture Ampion. See Use of Proceeds on page S-32 of this prospectus supplement.
Risk Factors	Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page S-12 of this prospectus supplement, and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus for a discussion of factors you should carefully consider before investing in our securities.

The number of shares of common stock to be outstanding immediately after this offering as reflected above is based on the actual number of shares outstanding as of September 25, 2013, which was 37,130,939 shares and excludes as of that date:

- Options representing the right to purchase a total of 5,474,065 shares of common stock at a weighted average exercise price of $2.71 per share;
- An aggregate of 1,621,808 additional shares of our common stock reserved for future issuance under our 2010 Stock Incentive Plan; and
- Warrants representing the right to purchase a total of 687,134 shares of common stock at a weighted average exercise price of $2.93 per share.

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RISK FACTORS

An investment in our common stock involves a high degree of risk. Before you make a decision to invest in our common stock, you should consider carefully the risks described below, together with other information in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein. Any of the following risks could have a material adverse effect on our business, operating results, prospects or financial condition. This could cause the trading price of our common stock to decline and you may lose all or part of your investment. These risks are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Related to Our Business

We have incurred significant losses since inception, expect to incur net losses for at least the next several years and may never achieve or sustain profitability.

We have experienced significant net losses since inception. As of June 30, 2013, we had an accumulated deficit of approximately $50.4 million. We expect our annual net losses to continue over the next several years as we advance our development programs and incur significant clinical development costs.

We have not received, and do not currently expect to receive, any revenues from the commercialization of our product candidates in the near term. In September 2011, we entered into a license, development and commercialization agreement with a major Korean pharmaceutical company with respect to Zertane in South Korea, which provided for a $500,000 upfront payment and future milestone payments that are contingent upon achievement of regulatory approvals and cumulative net sales targets. We may enter into additional licensing and collaboration arrangements, which may provide us with potential milestone payments and royalties and those arrangements, if obtained, will be our primary source of revenues for the coming years. We cannot be certain that any other licensing or collaboration arrangements will be concluded, or that the terms of those arrangements will result in our receiving material revenues. To obtain revenues from product candidates, we must succeed, either alone or with others, in a range of challenging activities, including completing clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we, or our collaborators, may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. We, and our collaborators, may never succeed in these activities and, even if we do, or one of our collaborators does, we may never generate revenues that are large enough for us to achieve profitability.

If we do not secure collaborations with strategic partners to test, commercialize and manufacture product candidates, we may not be able to successfully develop products and generate meaningful revenues.

A key aspect of our current strategy is to selectively enter into collaborations with third parties to conduct clinical testing, as well as to commercialize and manufacture product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators abilities to successfully perform the functions assigned to them in these arrangements. We currently have only one collaboration agreement in effect, which relates to Zertane in South Korea. Collaboration agreements typically call for milestone payments that depend on successful demonstration of efficacy and safety, obtaining regulatory approvals, and clinical trial results. Collaboration revenues are not guaranteed, even when efficacy and safety are demonstrated. The current economic environment may result in potential collaborators electing to reduce their external spending, which may prevent us from developing our product candidates.

Even if we succeed in securing collaborators, the collaborators may fail to develop or effectively commercialize products using our product candidates or technologies. Collaborations involving our product candidates pose a number of risks, including the following:

- collaborators may not have sufficient resources or decide not to devote the necessary resources due to internal constraints such as budget limitations, lack of human resources, or a change in strategic focus;

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collaborators may believe our intellectual property or the product candidate infringes on the intellectual property rights of others;

collaborators may dispute their responsibility to conduct development and commercialization activities pursuant to the applicable collaboration, including the payment of related costs or the division of any revenues;

collaborators may decide to pursue a competitive product developed outside of the collaboration arrangement;

collaborators may not be able to obtain, or believe they cannot obtain, the necessary regulatory approvals;

collaborators may delay the development or commercialization of our product candidates in favor of developing or commercializing another party s product candidate; or

collaborators may decide to terminate or not to renew the collaboration for these or other reasons.

Thus, collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. For example, our former collaborator that licensed Zertane conducted clinical trials which we believe demonstrated efficacy in treating premature ejaculation (PE), but the collaborator undertook a merger that we believe altered its strategic focus and thereafter terminated the collaboration agreement. The merger also created a potential conflict with a principal customer of the acquired company, which sells a product to treat PE in certain European markets.

Collaboration agreements are generally terminable without cause on short notice. Once a collaboration agreement is signed, it may not lead to commercialization of a product candidate. We also face competition in seeking out collaborators. If we are unable to secure new collaborations that achieve the collaborator s objectives and meet our expectations, we may be unable to advance our product candidates and may not generate meaningful revenues.

We will need substantial additional capital to fund our operations. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs and commercialization efforts.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We expect our expenses to increase in connection with our ongoing activities, particularly as we initiate new clinical trials of, initiate new research and preclinical development efforts for and seek marketing approval for, our product candidates. We will require additional capital to fund our operations, including to:

continue to fund clinical trials of Ampion and Optina;

prepare for and apply for regulatory a