Ampio Pharmaceuticals, Inc.
Form 10-K
February 14, 2014
**Table of Contents**

**UNITED STATES**

**SECURITIES AND EXCHANGE COMMISSION**

**Washington, D.C. 20549**

# FORM 10-K

**(Mark One)**

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the fiscal year ended December 31, 2013**

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**Commission File Number 333-146542**

**AMPIO PHARMACEUTICALS, INC.**

**(Exact Name of Registrant as Specified in Its Charter)**

| | |
|---|---|
| **Delaware** | **26-0179592** |
| **(State or other jurisdiction of** | **(I.R.S. Employer** |
| **incorporation or organization)** | **Identification Number)** |
| **5445 DTC Parkway** | |
| **Suite 925** | |
| **Greenwood Village, Colorado** | **80111** |
| **(Address of principal executive offices)** | **(Zip Code)** |

**(720) 437-6500**

**(Registrant s telephone number, including area code)**

**Securities registered pursuant to Section 12(b) of the Act: None**

**Securities registered pursuant to Section 12(g) of the Act: None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ¨ No x

Indicate by a check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports) and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the Registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K ¨

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definition of large accelerated filer , accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (check one):

| | |
|---|---|
| Large Accelerated Filer ¨ | Accelerated Filer x |

Non-Accelerated Filer ¨ (Do not check if a smaller reporting company) Smaller reporting company ¨
Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ¨ No x

The aggregate market value of common stock held by non-affiliates of the Registrant as of June 30, 2013 was $161,591,937.

Indicate the number of shares outstanding of each of the issuer s classes of common stock, as of the latest practicable date: As of February 12, 2014, 42,134,332 shares of common stock were outstanding.

Table of Contents

**TABLE OF CONTENTS**



This Report on Form 10-K refers to trademarks, such as Optina, Ampion, Zertane and Luoxis, which are protected under applicable intellectual property laws and are our property or the property of our subsidiaries. This Form 10-K also contains 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 Form 10-K 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.

*Unless otherwise indicated or unless the context otherwise requires, references in this Form 10-K to the "Company," "Ampio," "we," "us," or "our" are to Ampio Pharmaceuticals, Inc. and its subsidiaries; references to "Life Sciences" are to DMI Life Sciences, Inc., our predecessor; and references to "BioSciences" are to DMI BioSciences, Inc.*

Table of Contents

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

### Forward Looking Statements

This Annual Report on Form 10-K, or Annual Report, includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our anticipated future clinical and regulatory events, future financial position, business strategy and plans and objectives of management for future operations, are forward-looking statements. Forward looking statements are generally written in the future tense and/or are preceded by words such as may, will, should, forecast, could, expect, suggest, believe, estimate, continue, anticipate, intend, plan, or similar words, or the n terms or other variations on such terms or comparable terminology. Such forward-looking statements include, without limitation, statements regarding the anticipated start dates, durations and completion dates, as well as the potential future results, of our ongoing and future clinical trials, the anticipated designs of our future clinical trials, anticipated future regulatory submissions and events, the potential future commercialization of our product candidates, our anticipated future cash position and future events under our current and potential future collaborations. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including without limitation the risks described in Risk Factors in Part I, Item 1A of this Annual Report. These risks are not exhaustive. Other sections of this Annual Report include additional factors that could adversely impact our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. We assume no obligation to update or supplement forward-looking statements.

We obtained statistical data, market and product data, and forecasts used throughout this Form 10-K from market research, publicly available information and industry publications. While we believe that the statistical data, industry data and forecasts and market research are reliable, we have not independently verified the data, and we do not make any representation as to the accuracy of the information.

Table of Contents

**AMPIO PHARMACEUTICALS, INC.**

**PART I**

**Item 1.** ***Business***

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.

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 selected from Dr. Bar-Or s research based on certain criteria, particularly the ability to advance the candidates rapidly into late-stage clinical trials. The benchmarks used to build our pipeline were products with: (i) potential indications to address large underserved markets; (ii) strong intellectual property protection and the potential for market and data exclusivity; and (iii) a well-defined regulatory path to marketing approval.

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

We are also a majority shareholder in Luoxis, an in-vitro diagnostics company, and the sole shareholder of Vyrix Pharmaceuticals, a specialty pharmaceutical company. Luoxis novel diagnostic platform measures human Oxidation-Reduction Potential (ORP). Vyrix s therapeutic concentration is in men s health. We formed the subsidiaries to advance these proprietary technologies forward and provide a separate financing platform to fund development and commercialization and/or sale of these products.

**Corporate History**

Our predecessor, DMI Life Sciences, Inc. ( Life Sciences ), was formed by Michael Macaluso, our chief executive officer and chairman of our Board of Directors, and incorporated in Delaware in December 2008. Life Sciences did not conduct any business activity until April 16, 2009, at which time Life Sciences purchased certain assigned intellectual property (including 107 patents and pending patent applications, business products and tangible property) from DMI BioSciences, Inc. ( BioSciences ), a scientific discovery, privately-held Colorado corporation formed in May 1990 by Dr. David Bar-Or. Life Sciences issued 3,500,000 shares of our common stock to BioSciences, and assumed certain liabilities, as consideration for the assets purchased from BioSciences. In March 2010, Life Sciences merged with a subsidiary of Chay Enterprises, Inc. ( Chay ), a publicly-traded company incorporated in Colorado. Simultaneous with the merger, we changed our name to Ampio Pharmaceuticals, Inc. ( Ampio ), and reincorporated in Delaware. As a result of the Chay merger, we became a publicly-traded company and the outstanding Series A preferred stock of Life Sciences was converted into Life Sciences common stock, in accordance with Life Sciences amended and restated certificate of incorporation. For accounting and financial reporting purposes, Life Sciences was considered the acquirer and the Chay merger was treated as a reverse merger. All financial information presented in this Form 10-K for periods prior to the Chay merger reflects only that of Life Sciences, and does not reflect the

pre-merger Chay assets, liabilities, or operating results. In addition, all share, per share and related Life Sciences information has been adjusted to take into account the Chay merger.

On March 23, 2011, we acquired all of the outstanding stock of DMI BioSciences, Inc. ( BioSciences ) for 8,667,905 shares of our common stock (the merger stock ). We acquired BioSciences in order to obtain all rights to Zertane, BioScience s male sexual dysfunction drug for premature ejaculation ( PE ). As called for in the merger agreement, Ampio issued 405,066 shares of merger stock to holders of BioSciences in-the-money stock options and warrants, 500,000 shares of merger stock to holders of two BioSciences promissory notes in extinguishment of the notes, and placed 250,000 shares of merger stock in an indemnification escrow until December 31, 2011. The remaining 7,512,839 shares of merger stock were issued to the holders of BioSciences common stock on a pro rata basis. As required by the merger agreement, at the closing BioSciences donated back to Ampio s capital 3,500,000 shares of Ampio common stock formerly owned by BioSciences. Ampio separately issued 212,693 options in replacement of 250,850 BioSciences options that were out-of-the-money as of the date of execution of the merger agreement. On June 17, 2011, an additional 223,024 options were issued in exchange for 98,416 previously issued shares of Ampio stock pursuant to an agreement with three former BioSciences option holders. During 2011, we filed a claim on the indemnification escrow and were awarded 95,700 shares of Ampio stock to reflect the full value of the 223,024 options issued in exchange for the shares relinquished. On December 31, 2011 the remaining 154,300 indemnification escrow shares were allocated to the appropriate shareholders. All shares donated back, relinquished and escrow shares awarded to Ampio have been cancelled.

Table of Contents

**Our Product Pipeline**

**AMPION**

***Ampion for Osteoarthritis and Other Inflammatory Conditions***

Ampion is a sub 5000 molecular weight fraction of commercial human serum albumin ( HSA ). The primary constituent ingredient is aspartyl-alanyl diketopiperazine ( 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.

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 also 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.

***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 IA 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.

Table of Contents

***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. 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 either: (i) steroid, lidocaine, and saline; (ii) steroid, lidocaine, and Ampion, or; (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 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 for 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 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 at 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).

- 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).

***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 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 first trial would be a dose ranging trial, and 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 Pivotal 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, from baseline for Ampion compared to the same volume of saline. Secondary endpoints included evaluating safety and disease

Table of Contents

severity, as well as stiffness and function. Both Ampion dose cohorts experienced statistically significant reductions in pain compared to control, and there were no significant differences between the efficacy of the two Ampion doses. 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 -0.25 (95% CI: -0.41 to -0.08, p = 0.004).

- Patients receiving Ampion experienced, on average, a greater than 40% reduction in pain from baseline.

- Patients receiving Ampion achieved significantly greater reduction in pain, WOMAC A, across 12 weeks compared to saline vehicle control (p = 0.01)

- 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 Patient Global Assessment ( PGA ) of disease severity 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).

- Severe patients, defined as Kellgren-Lawrence IV, receiving Ampion achieved significantly greater reduction in pain, WOMAC A, from baseline to 12 weeks compared to severe patients receiving saline vehicle control (p = 0.017)

- 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 ).

On February 4, 2014, we announced that an article reporting the results was published in PLOSE ONE, an international, open-access, online publication. The article entitled: A Randomized Clinical Trial to Evaluate Two Doses of an Intra-Articular Injection of LMWF-5A in Adults with Pain Due to Osteoarthritis of the Knee details the efficacy and safety outcomes of the use of Ampion in the SPRING study.

We decided to follow 97 patients who were administered either 4 mL Ampion or saline vehicle control for an additional 8 weeks past the original 12 week primary endpoint. At week twenty, 50% of patients in the Kellgren-Lawrence grades of 3 and 4 (severe osteoarthritis) had improvement of 40% or more in the WOMAC A pain scale compared to 25% in the vehicle control group (p=0.04). Patients were also classified as responders if they achieved 40% or greater improvement in pain, WOMAC A, and function, WOMAC C, at and over 20 weeks after a single intra-articular injection into the knee. In these same grade 3 & 4 patients, there was a statistically significant

improvement in pain, WOMAC A, compared to the vehicle control both at week 20 (p=0.02) and over the whole period of 20 weeks (p=0.005). Also in these same grade 3 & 4 patients, there was a statistically significant improvement in function, WOMAC C, compared to vehicle control both at week 20 (p=0.05) and over the whole period of 20 weeks (p=0.04).

***Ongoing STEP Pivotal Trial***

On January 13, 2014, we announced the first patient injection in the Phase III final pivotal clinical trial of Ampion for the treatment of osteoarthritis of the knee. The Phase III STEP study has been designed to enroll 500 patients and the primary endpoint is reduction in pain for patients treated with Ampion compared to vehicle control at 12 weeks. STEP is a randomized, placebo-controlled, double-blind study in which patients with osteoarthritis knee pain will be randomized to receive either a 4 mL single injection of Ampion or saline control. The clinical effects of treatment on osteoarthritic pain will be evaluated during clinic visits at 6, 12, and 20 weeks using WOMAC Osteoarthritis Index and the PGA. Safety will be assessed by recording adverse events, concomitant medications, physical examination, vital signs and clinical laboratory tests. Topline results are anticipated in the third quarter of 2014.

***Manufacturing Facility***

On December 16, 2013, we announced a ten-year lease of a multi-purpose facility located in the Denver Metro Area. Renovation began in January 2014 and will provide commercial scale, FDA compliant, state-of-the-art, cGMP manufacturing of Ampion, an advanced research and development laboratory as well as a sufficient office space to consolidate all operations of the Company in a single facility. Ampio s new manufacturing facility will initially provide registration batches of Ampion supporting the BLA. Once the manufacturing operation is approved by the FDA for commercial production, the facility is expected to have an annual production capacity of approximately ten million doses of Ampion. More than 50% of the raw material, HSA, required to meet this capacity has already been secured through a long-term, non-exclusive, supply agreement. We anticipate that the new facility will be fully operational by summer 2014.

Table of Contents

***Future Development***

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.

**OPTINA**

***Optina for Diabetic Macular Edema***

Optina is a low-dose formulation of danazol that we are developing to treat diabetic macular edema ( DME ). Danazol is a synthetic derivative of modified testosterone ethisterone, and we believe it affects vascular endothelial cell linkage in a biphasic manner. At low doses, danazol decreases vascular permeability by increasing the barrier function of endothelial cells. The lipophilic low-molecular-weight weak androgen has the potential to treat multiple angiopathies.

Steroid hormones control a variety of functions through slow genomic and rapid non-genomic mechanisms. Danazol immediately increases intracellular cyclic adenosine monophosphate ( 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.

***Competition***

There are no orally administered treatments for DME currently available nor to our knowledge are any being tested in clinical trials. The current standard of care in the U.S. for the treatment of DME is laser photocoagulation. The first and only approved therapy in the U.S. is intravitreal ranibizumab-injections. Ranibizumab belongs to a therapeutic class inhibiting vascular endothelial growth factor ( 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 pending approval in the United States while its sponsor reportedly resolves manufacturing issues. Dexamethasone intravitr eal implant is available in the U.S. for macular edema following retinal vein occlusion and noninfectious uveitis and the product s sponsor has submitted for U.S. and European approval in the treatment of DME. Aflibercept, another anti-VEGF antibody treatment, is also awaiting U.S. and European approval in the treatment of DME.

Table of Contents

***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) which were treated orally with either one of three 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 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 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 15 mg BID achieved significant reduction in CRT (96.24 microns; p=0.01).

Patients stratified around a BMI of 26 receiving Optina 5 mg 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 Trials in Support of a §505(b)(2) New Drug Application ( 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. Patients are randomized (1:1:1) to receive one of two oral doses of Optina, 0.5 mg per BMI and 1.0 mg 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 have enrolled over 300 patients and expect enrollment to be completed in the first quarter of 2014. 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 was determined by an interim analysis occurring at week 4 involving approximately 150 patients. We announced in October 2013 that an independent data review committee ( IDRC ) recommended the continuation of the study after an unmasked interim analysis which found that there was a treatment dosage demonstrating a potentially beneficial anatomic effect, and there were no significant safety concerns. Based on the favorable outcome of the interim analysis, Ampio initiated an open label extension study for those patients who have completed the trial and wish to remain on Optina and offer patients who received placebo in the primary study a chance to cross-over to undergo treatment with the active treatment.

***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.

Table of Contents

***NCE 001***

Para-phenoxy-methylphenidate is a novel, small molecule methylphenidate derivative. Its basic mechanism of action is believed to be to increase methylation of the catalytic sub unit of Protein Phosphatase 2 A ( 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.

**Subsidiaries**

***Luoxis Diagnostics, Inc.***

Ampio owns 80.9% of Luoxis. Luoxis is an in-vitro diagnostics company focused on the development and global commercialization of RedoxSYS . This novel, diagnostic platform is comprised of a first-in-class, point-of-care device and disposable, testing strips that together measure the presence of oxidative stress and antioxidant reserves. To our knowledge, RedoxSYS is the only in-vitro diagnostic platform that measures human Oxidation-Reduction Potential ( 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.

***Vyrix Pharmaceuticals, Inc.***

Vyrix Pharmaceuticals was formed on November 18, 2013 and is 100% owned by Ampio. Vyrix is a specialty pharmaceutical focused on developing and commercializing late-stage prescription pharmaceuticals to improve men s health and quality of life. The Company s most advanced product is Zertane an oral drug in late stage development as treatment for PE. PE is a condition that has major impact on the quality of life for millions of men and their sexual partners. Vyrix is also developing a combination product with Zertane and an erectile dysfunction product to address co-morid PE and erectile dysfunction ( ED ).

**Government Regulation**

***FDA Approval Process***

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, or the FDC Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending NDAs, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

Pharmaceutical and biologic product development in the US typically involves the performance of satisfactory preclinical laboratory and animal studies under the FDA s Good Laboratory Practices ( GLPs ) regulation, the development and demonstration of manufacturing processes which conform to FDA mandated current good manufacturing practices, or cGMP, a quality system regulating manufacturing, the submission and acceptance of an IND application which must become effective before human clinical trials may begin in the US, obtaining the

approval of Institutional Review Boards ( IRBs ) at each site where we plan to conduct a clinical trial to protect the welfare and rights of human subjects in clinical trials, adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug or biologic for each indication for which FDA approval is sought, and the submission to the FDA for review and approval of a NDA or BLA. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the product or disease.

Preclinical tests generally include laboratory evaluation of a product candidate, its chemistry, formulation, stability and toxicity, as well as certain animal studies to assess its potential safety and efficacy. Results of these preclinical tests, together with manufacturing information (in compliance with GLP and cGMP), analytical data and the clinical trial protocol (detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated), must be submitted to the FDA as part of an IND, which must become effective before human clinical trials can begin.

An IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the intended conduct of the trials and imposes what is referred to as a clinical hold. Preclinical studies

Table of Contents

generally take several years to complete, and there is no guarantee that an IND based on those studies will become effective, allowing clinical testing to begin. In addition to FDA review of an IND, each medical site that desires to participate in a proposed clinical trial must have the protocol reviewed and approved by an independent IRB or Ethics Committee ( EC ). The IRB considers, among other things, ethical factors, and the selection and safety of human subjects. Clinical trials must be conducted in accordance with the FDA s Good Clinical Practices ( GCP ) requirements. The FDA and/or IRB/EC may order the temporary, or permanent, discontinuation of a clinical trial or a specific clinical trial site to be halted at any time, or impose other sanctions for failure to comply with requirements under the appropriate entity jurisdiction.

Clinical Trials to support NDAs and BLAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1 clinical trials, a product candidate is typically introduced either into healthy human subjects or patients with the medical condition for which the new drug is intended to be used. The main purpose of the trial is to assess a product candidate s safety and the ability of the human body to tolerate the product candidate. Phase 1 clinical trials generally include less than 50 subjects or patients. During Phase II trials, a product candidate is studied in an exploratory trial or trials in a limited number of patients with the disease or medical condition for which it is intended to be used in order to: (i) further identify any possible adverse side effects and safety risks, (ii) assess the preliminary or potential efficacy of the product candidate for specific target diseases or medical conditions, and (iii) assess dosage tolerance and determine the optimal dose for Phase 3 trial. Phase 3 trials are generally undertaken to demonstrate clinical efficacy and to further test for safety in an expanded patient population with the goal of evaluating the overall risk-benefit relationship of the product candidate. Phase 3 trials will generally be designed to reach a specific goal or endpoint, the achievement of which is intended to demonstrate the candidate product s clinical efficacy and adequate information for labeling of the drug or biologic.

After completion of the required clinical testing, a NDA or BLA is prepared and submitted to the FDA. FDA approval of the NDA or BLA is required before marketing of the product may begin in the U.S. The NDA must include the results of all preclinical, clinical, and other testing and a compilation of data relating to the product s pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting a NDA is substantial. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee, currently exceeding $1.8 million and the manufacturer and/or sponsor under an approved NDA are also subject to annual product and establishment user fees, currently approximately $0.1 million per product and $0.5 million per establishment. These fees are typically increased annually.

The FDA has 60 days from its receipt of a NDA to determine whether the application will be accepted for filing based on the FDA s threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Most such applications for standard review drug products are reviewed within ten months; most applications for priority review drugs are reviewed in six months. The review process for both standard and priority review may be extended by FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission. The FDA may also refer applications for novel drug products, or drug products which present difficult questions of safety or efficacy, to an advisory committee typically a panel that includes clinicians and other experts for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving a NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. The FDA will not approve the product unless compliance with cGMP is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA s satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug s safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

***Fast Track Designation***

The FDA has developed Fast Track policies, which provide the potential for expedited review of a NDA. Fast Track status is potentially provided only for those new and novel therapies that are intended to treat persons with life-threatening and severely

Table of Contents

debilitating diseases where there is a defined unmet medical need, especially where no satisfactory alternative therapy exists or the new therapy is significantly superior to alternative therapies. During the development of product candidates that qualify for this status, the FDA may expedite consultations and reviews of these experimental therapies. Fast Track status also provides the potential for a product candidate to have a Priority Review. A Priority Review allows for portions of the NDA to be submitted to the FDA for review prior to the completion of the entire application, which could result in a reduction in the length of time it would otherwise take the FDA to complete its review of the NDA. Fast Track status may be revoked by the FDA at any time if the clinical results of a trial fail to continue to support the assertion that the respective product candidate has the potential to address and unmet medical need. For biologics, priority review is further limited only for therapies intended to treat a serious or life threatening disease.

***Orphan Drug Designation***

The FDA may grant Orphan Drug status to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States. If and when the FDA grants Orphan Drug status, the generic name and trade name of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Aside from guidance concerning the non-clinical laboratory studies and clinical investigations necessary for approval of the NDA, Orphan Drug status does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The FDA may grant Orphan Drug status to multiple competing product candidates targeting the same indications. A product that has been designated as an Orphan Drug that subsequently receives the first FDA approval is entitled to Orphan Drug exclusivity. This exclusivity means the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years from the date of the initial FDA approval. Orphan Drug approval may also provide certain tax benefits to the company that receives the first FDA approval. Finally, the FDA may fund the development of orphan products through its grants program for clinical studies.

***Breakthrough Designation***

Breakthrough therapy designation is intended to expedite the development and review of drugs for serious or life-threatening conditions. The criteria for breakthrough therapy designation require preliminary clinical evidence that demonstrates the drug may have substantial improvement for at least one clinically significant endpoint compared to available therapy. A breakthrough therapy designation conveys all of the fast track program features, as well as more intensive FDA guidance on an efficient drug development program. The FDA also has an organizational commitment to involve senior management in such guidance.

***Accelerated Approval***

Under the FDA s accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients compared to existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. In clinical trials, a surrogate endpoint is a measurement of laboratory tests or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions, or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the predictability of surrogate endpoints for clinical outcomes. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

***Foreign Regulatory Approval***

Outside of the United States, our ability to market our product candidates will be contingent upon our receiving marketing authorizations from the appropriate foreign regulatory authorities, whether or not FDA approval has been obtained. The foreign regulatory approval process in most industrialized countries generally encompasses risks similar to those we will encounter in the FDA approval process. The requirements governing conduct of clinical trials and marketing authorizations, and the time required to obtain requisite approvals, may vary widely from country to country and differ from that required for FDA approval.

Under European Union regulatory systems, marketing authorizations may be submitted either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval. The mutual recognition process results in separate national marketing authorizations in the reference member state and each concerned member state. We will seek to choose the appropriate route of European regulatory filing in an attempt to accomplish the most rapid regulatory approvals for our product candidates when ready for review. However, the chosen regulatory strategy may not secure regulatory approvals or approvals of the chosen product indications. In addition, these approvals, if obtained, may take longer than anticipated. We can provide no assurance that any of our product candidates will prove to be safe or effective, will receive required regulatory approvals, or will be successfully commercialized.

Table of Contents

***The Hatch-Waxman Act***

In seeking approval for a drug through a NDA, applicants are required to list with the FDA each patent whose claims cover the applicant s product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA s Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ( ANDA ). An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, pre-clinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as generic equivalents to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA s Orange Book. Specifically, the applicant must certify that: 1) the required patent information has not been filed; 2) the listed patent has expired; 3) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or 4) the listed patent is invalid or will not be infringed by the new product. A certification that the new product will not infringe the already approved product s listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any non-patent exclusivity listed in the Orange Book for the referenced product has expired. Federal law provides a period of five years following approval of a drug containing no previously approved active ingredients during which ANDAs for generic versions of those drugs cannot be submitted, unless the submission contains a Paragraph IV challenge to a listed patent in which case the submission may be made four years following the original product approval. Federal law provides for a period of three years of exclusivity during which FDA cannot grant effective approval of an ANDA based on the approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage form, route of administration or combination, or for a new use; the approval of which was required to be supported by new clinical trials conducted by, or for, the applicant.

***Post-Approval Regulation***

Even if a product candidate receives regulatory approval, the approval is typically limited to specific clinical indications. Further, even after regulatory approval is obtained, subsequent discovery of previously unknown problems with a product may result in restrictions on its use or even complete withdrawal of the product from the market. Any FDA-approved products manufactured or distributed by us are subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse events or experiences. Further, drug manufacturers and their subcontractors are required to register their establishments with the FDA and state agencies, and are subject to periodic inspections by the FDA and state agencies for compliance with cGMP, which impose

rigorous procedural and documentation requirements upon us and our contract manufacturers. We cannot be certain that we or our present or future contract manufacturers or suppliers will be able to comply with cGMP regulations and other FDA regulatory requirements. Failure to comply with these requirements may result in, among other things, total or partial suspension of production activities, failure of the FDA to grant approval for marketing, and withdrawal, suspension, or revocation of marketing approvals.

If the FDA approves one or more of our product candidates, we and the contract manufacturers we use for manufacture of clinical supplies and commercial supplies must provide certain updated safety and efficacy information. Product changes, as well as certain changes in the manufacturing process or facilities where the manufacturing occurs or other post-approval changes may necessitate additional FDA review and approval. The labeling, advertising, promotion, marketing and distribution of a drug or biologic product also must be in compliance with FDA and Federal Trade Commission ( FTC ) requirements which include, among others, standards and regulations for direct-to-consumer advertising, off-label promotion, industry sponsored scientific and educational activities, and promotional activities involving the Internet. The FDA and FTC have very broad enforcement authority, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing us to correct deviations from regulatory standards and enforcement actions that can include seizures, fines, injunctions and criminal prosecution.

Table of Contents

**Intellectual Property Summary**

***Ampion***

As of December 31, 2013, the current Ampion patent portfolio consists of 44 issued patents and 42 pending applications worldwide. The portfolio primarily consists of three 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.

The second family includes five 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, Korea and Hong Kong. The standard 20-year expiration for patents in this family is in 2024.

The third family includes one pending United States application and a Patent Cooperation Treaty ( PCT ) international application with claims directed to the use of DA-DKP for the treatment of degenerative joint diseases. The standard 20-year expiration for patents in this family is in 2032.

***Optina***

As of December 31, 2013, the Optina patent portfolio currently consists of 40 issued patents and 47 pending applications worldwide. The portfolio consists primarily of three patent families, the first and second of which include claims for the use of low doses of danazol to treat conditions associated with vascular hyperpermeability. These two families include one issued patent in each of the U.S., EPO (validated in 36 countries and Hong Kong) and Canada with claims relating to methods of treating macular edema with danazol. These families also include pending applications in Australia, Brazil, China, Eurasian Patent Organization, EPO, Indonesia, Israel, Japan, Korea, Mexico, Malaysia, New Zealand, Philippines, Singapore, Hong Kong and South Africa and the United States. The standard 20-year expiration for patents in these families is in 2030. The third family is for the treatment of conditions associated with vascular hyperpermeability with low doses of danazol that correspond to the body fat content of the patient. The standard 20-year expiration for patents in this family is in 2033.

***Luoxis***

As of December 31, 2013, the current Luoxis patent portfolio consists of 32 issued patents and 31 pending applications worldwide. The portfolio primarily consists of four families filed in the United States and throughout the world. The first family includes two issued patents and six pending applications with claims directed to the measurement of the oxidation reduction potential (ORP) of a patient sample to evaluate various conditions. The standard 20-year expiration for patents in this family is in 2028. The second family includes three pending United States applications and a PCT international application with claims directed to the measurement of the ORP capacity of a patient sample to evaluate various conditions. The standard 20-year expiration for patents in this family is in 2033.

The third family includes four issued patents and 15 pending applications with claims directed to devices and methods for the measurement of ORP and ORP capacity. The standard 20-year expiration for patents in this family is in 2032.

The fourth family includes one pending United States application and a PCT international application with claims directed to multiple layer gel test strip measurement devices and methods of making for use in measuring ORP and ORP capacity. The standard 20-year expiration for patents in this family is in 2033.

***Vyrix Pharmaceuticals***

As of December 31, 2013, the current Vyrix patent portfolio consists of 73 issued patents and 19 pending applications worldwide. The portfolio primarily consists of three families filed in the United States and throughout the world. The first family includes 29 issued patents for the use of tramadol to treat premature ejaculation. The standard 20-year expiration for patents in this family is in 2022. The other two families are for the use of a combination of tramadol and a phosphodiesterase inhibitor to treat comorbid premature ejaculation and erectile dysfunction and to treat sexual dysfunction side effects associated with administration of tramadol. These two families include issued patents in Europe, Canada, China, Mexico, New Zealand, and South Africa and pending applications in the United States, Australia, Brazil, China, India, Japan, Korea, and the Philippines. The standard 20-year expiration for patents in these families is in 2028.

Table of Contents

***Barriers of Entry General***

We also maintain trade secrets and proprietary know-how that we seek to protect through confidentiality and nondisclosure agreements. We expect to seek United States and foreign patent protection for drug and diagnostic products we discover, as well as therapeutic and diagnostic products and processes. We expect also to seek patent protection or rely upon trade secret rights to protect certain other technologies which may be used to discover and characterize drugs and diagnostic products and processes, and which may be used to develop novel therapeutic and diagnostic products and processes. These agreements may not provide meaningful protection or adequate remedies in the event of unauthorized use or disclosure of confidential and proprietary information. If we do not adequately protect our trade secrets and proprietary know-how, our competitive position and business prospects could be materially harmed.

The patent positions of companies such as ours involve complex legal and factual questions and, therefore, their enforceability cannot be predicted with any certainty. Our issued and licensed patents, and those that may be issued to us in the future, may be challenged, invalidated or circumvented, and the rights granted under the patents or licenses may not provide us with meaningful protection or competitive advantages. Our competitors may independently develop similar technologies or duplicate any technology developed by us, which could offset any advantages we might otherwise realize from our intellectual property. Furthermore, even if our product candidates receive regulatory approval, the time required for development, testing, and regulatory review could mean that protection afforded us by our patents may only remain in effect for a short period after commercialization. The expiration of patents or license rights we hold could adversely affect our ability to successfully commercialize our pharmaceutical drugs or diagnostics, thus harming our operating results and financial position.

We will be able to protect our proprietary intellectual property rights from unauthorized use by third parties only to the extent that such rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. If we must litigate to protect our intellectual property from infringement, we may incur substantial costs and our officers may be forced to devote significant time to litigation-related matters. The laws of certain foreign countries do not protect intellectual property rights to the same extent as do the laws of the United States.

Our pending patent applications, or those we may file or license from third parties in the future, may not result in patents being issued. Until a patent is issued, the claims covered by an application for patent may be narrowed or removed entirely, thus depriving us of adequate protection. As a result, we may face unanticipated competition, or conclude that without patent rights the risk of bringing product candidates to market exceeds the returns we are likely to obtain. We are generally aware of the scientific research being conducted in the areas in which we focus our research and development efforts, but patent applications filed by others are maintained in secrecy for at least 18 months and, in some cases in the United States, until the patent is issued. The publication of discoveries in scientific literature often occurs substantially later than the date on which the underlying discoveries were made. As a result, it is possible that patent applications for products similar to our drug or diagnostic candidates may have already been filed by others without our knowledge.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights, and it is possible that our development of product candidates could be challenged by other pharmaceutical or biotechnology companies. If we become involved in litigation concerning the enforceability, scope and validity of the proprietary rights of others, we may incur significant litigation or licensing expenses, be prevented from further developing or commercializing a product candidate, be required to seek licenses that may not be available from third parties on commercially acceptable terms, if at all, or subject us to compensatory or punitive damage awards. Any of these consequences could materially harm our business.

**Competition**

The biotechnology and pharmaceutical industries are highly competitive and subject to significant and rapid technological change as researchers learn more about diseases and develop new technologies and treatments. Significant competitive factors in our industry include product efficacy and safety; quality and breadth of an organization s technology; skill of an organization s employees and its ability to recruit and retain key employees; timing and scope of regulatory approvals; government reimbursement rates for, and the average selling price of, products; the availability of raw materials and qualified manufacturing capacity; manufacturing costs; intellectual property and patent rights and their protection; and sales and marketing capabilities.

We cannot assure you that any of our products that we successfully develop will be clinically superior or scientifically preferable to products developed or introduced by our competitors.

Many of our actual and potential competitors have substantially longer operating histories and possess greater name recognition, product portfolios, and significantly greater experience in discovering, developing, manufacturing, and marketing products as well as financial, research, and marketing resources than us. Among our smaller competitors, many of these companies have established co-development and collaboration relationships with larger pharmaceutical and biotechnology firms, which may make it more difficult

Table of Contents

for us to attract strategic partners. Our current and potential competitors include major multinational pharmaceutical companies, biotechnology firms, universities and research institutions. Some of these companies and institutions, either alone or together with their collaborators, have substantially greater financial resources and larger research and development staffs than do we. In addition, many of these competitors, either alone or together with their collaborators, have significantly greater experience than us in discovering, developing, manufacturing, and marketing pharmaceutical products and diagnostics. If one of our competitors realizes a significant advance in pharmaceutical drugs or diagnostics that address one or more of the diseases targeted by our product candidates, our products or diagnostics could be rendered uncompetitive or obsolete.

Our competitors may also succeed in obtaining FDA or other regulatory approvals for their product candidates more rapidly than we are able to do, which could place us at a significant competitive disadvantage or deny us marketing exclusivity rights. Market acceptance of our product or diagnostic candidates will depend on a number of factors, including: (i) potential advantages over existing or alternative therapies or tests, (ii) the actual or perceived safety of similar classes of products, (iii) the effectiveness of sales, marketing, and distribution capabilities, and (iv) the scope of any approval provided by the FDA or foreign regulatory authorities.

Although we believe our product candidates possess attractive attributes, we cannot assure you that our product candidates will achieve regulatory or market acceptance, or that we will be able to compete effectively in the pharmaceutical drug or diagnostic markets. If our product candidates fail to gain regulatory approvals and acceptance in their intended markets, we may not generate meaningful revenues or achieve profitability.

**Research and Development**

Our strategy is to minimize fixed overhead by outsourcing much of our research and development activities. Through a sponsored research agreement, our discovery activities are conducted by Trauma Research LLC, or TRLLC, a limited liability company owned by Dr. David Bar-Or. Under the research agreement, TRLLC conducts drug and biomarker discovery and development programs at its research facilities, and we provide funding and some scientific personnel. Intellectual property from discovery programs conducted by TRLLC on our behalf belongs to us, and we are solely responsible for protecting that intellectual property. While we have the right to generally request development work under the research agreement, TRLLC directs such work and is responsible for how the work is performed.

For the years ended December 31, 2013, 2012 and 2011, we recorded $18.3 million, $7.5 million, and $6.6 million, respectively, of research and development expenses. Research and development expenses represented 76%, 63.1 %, and 59.6% of total operating expenses in the years ended December 31, 2013, 2012 and 2011, respectively. More information regarding our research and development activities can be found in the section entitled Management s Discussion and Analysis of Financial Condition and Results of Operations under Item 7 of this Annual Report.

**Manufacturing**

On December 16, 2013, we announced a ten-year lease of a multi-purpose facility located in the Denver Metro Area. Renovation began in January 2014 and will provide commercial scale, FDA compliant, state-of-the-art, GMP manufacturing of Ampion, an advanced research and development laboratory as well as a sufficient office space to consolidate all operations of the Company in a single facility. Ampio s new manufacturing facility will initially provide registration batches of Ampion supporting the BLA. Once the manufacturing operation is approved by the FDA for commercial production, the facility will have an annual production capacity of approximately ten million doses of Ampion. More than 50% of the raw material, human serum albumin or HSA, required to meet this capacity has already been secured through a long-term, non-exclusive, supply agreement as previously announced. We

anticipate that the new facility will be fully operational by summer 2014.

Our business strategy for Optina is to use cGMP compliant contract manufacturers for manufacture of clinical supplies as well as for commercial supplies if required by our commercialization plans, and to transfer manufacturing responsibility to our collaboration partners when possible.

**Compliance with Environmental Laws**

We believe we are in compliance with current material environmental protection requirements that apply to us or our business. Costs attributable to environmental compliance are not currently material.

**Product Liability and Insurance**

The development, manufacture and sale of pharmaceutical products involve inherent risks of adverse side effects or reactions that can cause bodily injury or even death. Product candidates we succeed in commercializing could adversely affect consumers even after obtaining regulatory approval and, if so, we could be required to withdraw a product from the market or be subject to administrative or other proceedings. As we are not now manufacturing, marketing or distributing pharmaceutical products or diagnostics, we have

Table of Contents

elected not to obtain product liability insurance at the current time. We obtain clinical trial liability coverage for human clinical trials, and will obtain appropriate product liability insurance coverage for products we manufacture and sell for human consumption. The amount, nature and pricing of such insurance coverage will likely vary due to a number of factors such as the product candidate s clinical profile, efficacy and safety record, and other characteristics. We may not be able to obtain sufficient insurance coverage to address our exposure to product recall or liability actions, or the cost of that coverage may be such that we will be limited in the types or amount of coverage we can obtain. Any uninsured loss we suffer could materially and adversely affect our business and financial position.

**Employees**

As of February 14, 2014, we had 16 full-time employees and utilized the services of a number of consultants on a temporary basis. Overall, we have not experienced any work stoppage and do not anticipate any work stoppage in the foreseeable future. Management believes that relations with our employees are good.

**Available Information**

Our principal executive offices are located at 5445 DTC Parkway, Suite 925, Greenwood Village, Colorado 80111 USA, and our phone number is (720) 437-6500.

We maintain a website on the internet at *www.ampiopharma.com*. We make available free of charge through our website, by way of a hyperlink to a third-party site that includes filings we make with the SEC website (*www.sec.gov)*, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports electronically filed or furnished pursuant to Section 15(d) of the Exchange Act. The information on our website is not, and shall not be deemed to be, a part of this annual report on Form 10-K or incorporated into any other filings we make with the SEC. In addition, the public may read and copy any materials we file with the SEC at the SEC s Public Reference Room at 100 F Street, N.E., Washington D.C., 20549. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330. Our Code of Conduct and Ethics and the charters of our Nominating and Governance Committee, Audit Committee, and Compensation Committee of our Board of Directors may be accessed within the Investor Relations section of our website. Amendments and waivers of the Code of Conduct and Ethics will also be disclosed within four business days of issuance on the website. Information found in our website is neither part of this annual report on Form 10-K nor any other report filed with the SEC.

## Item 1A. *Risk Factors*

### 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 December 31, 2013, we had an accumulated deficit of approximately $64 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 succeed in these activities, and may never generate revenues that are significant enough 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

Table of Contents

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;
- 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 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 approval for our product candidates;
- further develop and assess the clinical utility of the oxidation reduction potential (ORP) diagnostic device, or the ORP device;
- develop additional product candidates;
- conduct additional clinical research and development;
- pursue existing and new claims covered by intellectual property we own or license; and
- sustain our corporate overhead requirements, and hire and retain necessary personnel.

Until we can generate revenue from collaboration agreements to finance our cash requirements, which we may not accomplish, we expect to finance future cash needs primarily through offerings of our debt or equity securities. We currently have only one collaboration agreement in effect, which relates to Zertane in South Korea.

We do not know whether additional funding will be available to us on acceptable terms, or at all. If we are unable to secure additional funding when needed, we may have to delay, reduce the scope, or eliminate development of one or more of our product candidates, or substantially curtail or close our operations altogether. Alternatively, we may have to obtain a collaborator for one or more of our product candidates at an earlier stage of development, which could lower the economic value of those product candidates to us.

Table of Contents

***Ampion, Optina and our ORP Device are currently undergoing, or are expected to undergo, clinical trials that are time-consuming and expensive, the outcomes of which are unpredictable, and for which there is a high risk of failure. If clinical trials of our product candidates fail to satisfactorily demonstrate safety and efficacy to the FDA and other regulators, we, or our collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.***

Pre-clinical testing and clinical trials are long, expensive and unpredictable processes that can be subject to extensive delays. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. It may take several years to complete the pre-clinical testing and clinical development necessary to commercialize a drug or biologic, and delays or failure can occur at any stage. Interim results of clinical trials do not necessarily predict final results, and success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials even after promising results in earlier trials and we cannot be certain that we will not face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced.

Our product development programs are at various stages of development. We continue to work toward completion and analysis of clinical trials for our two primary products: Ampion and Optina, as well as for the ORP device. An unfavorable outcome in one or more trials for Ampion, Optina or the ORP Device would be a major set-back for the development programs for these product candidates and for us. Due to our limited financial resources, an unfavorable outcome in one or more of these trials may require us to delay, reduce the scope of, or eliminate one of these product development programs, which could have a material adverse effect on our business and financial condition and on the value of our common stock.

In connection with clinical testing and trials, we face a number of risks, including:

- a product candidate is ineffective, inferior to existing approved medicines, unacceptably toxic, or has unacceptable side effects;
- patients may die or suffer other adverse effects for reasons that may or may not be related to the product candidate being tested;
- the results may not confirm the positive results of earlier testing or trials; and
- the results may not meet the level of statistical significance required by the U.S. Food and Drug Administration, or FDA, or other regulatory agencies to establish the safety and efficacy of our product candidates.

The results of pre-clinical studies do not necessarily predict clinical success, and larger and later-stage clinical studies may not produce the same results as earlier-stage clinical studies. Frequently, product candidates developed by pharmaceutical companies have shown promising results in early pre-clinical or clinical studies, but have subsequently suffered significant setbacks or failed in later clinical studies. In addition, clinical studies of potential products often reveal that it is not possible or practical to continue development efforts for these product candidates.

If we do not successfully complete pre-clinical and clinical development, we will be unable to market and sell products derived from our product candidates and generate revenues. Even if we do successfully complete clinical trials, those results are not necessarily predictive of results of additional trials that may be needed before an NDA or BLA may be submitted to the FDA. Although there are a large number of drugs and biologics in development in the U.S. and other countries, only a small percentage result in the submission of an NDA or BLA to the FDA, even fewer are approved for commercialization, and only a small number achieve widespread physician and consumer acceptance following regulatory approval. If our clinical studies are substantially delayed or fail to prove the safety and effectiveness of our product candidates in development, we may not receive regulatory approval of any of these product candidates and our business and financial condition will be materially harmed.

***Delays, suspensions and terminations in our clinical trials could result in increased costs to us and delay or prevent our ability to generate revenues.***

Human clinical trials are very expensive, time-consuming, and difficult to design, implement and complete. We currently expect clinical trials of our product candidates could take from six to 24 months to complete, but the completion of trials for our product candidates may be delayed for a variety of reasons, including delays in:

demonstrating sufficient safety and efficacy to obtain regulatory approval to commence a clinical trial;

reaching agreement on acceptable terms with prospective contract research organizations and clinical trial sites;

manufacturing sufficient quantities of a product candidate;

obtaining approval of an IND from the FDA;

obtaining institutional review board approval to conduct a clinical trial at a prospective clinical trial site;

Table of Contents

determining dosing and making related adjustments; and

patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical trial sites, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial.

The commencement and completion of clinical studies for our product candidates may be delayed, suspended or terminated due to a number of factors, including:

lack of effectiveness of product candidates during clinical studies;

adverse events, safety issues or side effects relating to the product candidates or their formulation;

inability to raise additional capital in sufficient amounts to continue clinical trials or development programs, which are very expensive;

the need to sequence clinical studies as opposed to conducting them concomitantly in order to conserve resources;

our inability to enter into collaborations relating to the development and commercialization of our product candidates;

failure by us or our collaborators to conduct clinical trials in accordance with regulatory requirements;

our inability or the inability of our collaborators to manufacture or obtain from third parties materials sufficient for use in pre-clinical and clinical studies;

governmental or regulatory delays and changes in regulatory requirements, policy and guidelines, including mandated changes in the scope or design of clinical trials or requests for supplemental information with respect to clinical trial results;

failure of our collaborators to advance our product candidates through clinical development;

delays in patient enrollment, variability in the number and types of patients available for clinical studies, and lower than anticipated retention rates for patients in clinical trials;

difficulty in patient monitoring and data collection due to failure of patients to maintain contact after treatment;

a regional disturbance where we or our collaborative partners are enrolling patients in our clinical trials, such as a pandemic, terrorist activities or war, or a natural disaster; and

varying interpretations of data by the FDA and similar foreign regulatory agencies.

Many of these factors may also ultimately lead to denial of regulatory approval of a current or potential product candidate. If we experience delay, suspensions or terminations in a clinical trial, the commercial prospects for the related product candidate will be harmed, and our ability to generate product revenues will be delayed. We cannot be certain we will successfully complete the Phase III Ampion and §505(b)(2) Optina trials within any specific time period, if at all.

In addition, we may encounter delays or product candidate rejections based on new governmental regulations, future legislative or administrative actions, or changes in FDA policy or interpretation during the period of product development. If we obtain required regulatory approvals, such approvals may later be withdrawn. Delays or failures in obtaining regulatory approvals may:

adversely affect the commercialization of any product candidates we develop;

diminish any competitive advantages that such product candidates may have or attain.

Furthermore, if we fail to comply with applicable FDA and other regulatory requirements at any stage during this regulatory process, we may encounter or be subject to:

delays in clinical trials or commercialization;

refusal by the FDA to review pending applications or supplements to approved applications;

product recalls or seizures;

suspension of manufacturing;

withdrawals of previously approved marketing applications; and

fines, civil penalties, and criminal prosecutions.

***If our product candidates are not approved by the FDA, we will be unable to commercialize them in the United States.***

The FDA must approve any new medicine before it can be commercialized, marketed, promoted or sold in the United States. We must provide the FDA with data from pre-clinical and clinical studies that demonstrate that our product candidates are safe and effective for a defined indication before they can be approved for commercial distribution. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We will not obtain approval for a product candidate unless and until the FDA approves a NDA for a drug and a BLA for a biologic. The processes by which regulatory approvals are obtained from the FDA to market and sell a new or repositioned product are complex, require a number of years and involve the expenditure of substantial resources. We cannot assure you that any of our product candidates will receive FDA approval in the future, and the time for receipt of any such approval is currently incapable of estimation.

Table of Contents

***We or our collaborators intend to seek FDA approval for most of our product candidates using an expedited process established by the FDA. If we, or our collaborators, are unable to secure clearances to use expedited development pathways from the FDA for certain of our drug product candidates, we, or they, may be required to conduct additional pre-clinical studies or clinical trials beyond those that we, or they, contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals and of any product revenues.***

Assuming successful completion of clinical trials, we expect to submit NDAs to the FDA at various times in the future under §505(b)(2) of the Food, Drug and Cosmetic Act, as amended, or the FDCA. NDAs submitted under this section are eligible to receive FDA approval by relying in part on the FDA s findings of safety and efficacy for a previously approved drug. We are currently pursuing in our clinical trials a §505(b)(2) pathway for Optina and may also do so for other product candidates. The FDA s 1999 guidance on §505(b)(2) applications states that new indications for a previously approved drug, a new combination product, a modified active ingredient, or changes in dosage form, strength, formulation, and route of administration of a previously approved product are encompassed within the §505(b)(2) NDA process. Relying on §505(b)(2) is advantageous because we or our collaborators may not be required (i) to perform the full range of safety and efficacy trials that is otherwise required to secure approval of a new drug, and (ii) obtain a right of reference from the applicant that obtained approval of the previously approved drug. However, a §505(b)(2) application must support the proposed change of the previously approved drug by including necessary and adequate information, as determined by the FDA, and the FDA may still require us to perform a full range of safety and efficacy trials.

If one of our product candidates achieves clinical trial objectives, we must prepare and submit to the FDA a comprehensive NDA or BLA application. Review of the application may lead the FDA to request more information or require us to perform additional clinical trials, thus adding to product development costs and delaying any marketing approval from the FDA. Additionally, time to review may vary significantly based on the disease to be treated, availability of alternate treatments, severity of the disease, and the risk/benefit profile of the proposed product. Even if one of our products receives FDA marketing approval, we could be required to conduct post-marketing Phase IV studies and surveillance to monitor for adverse effects. If we experience delays in NDA application processing, requests for additional information or further clinical trials, or are required to conduct post-marketing studies or surveillance, our product development costs could increase substantially, and our ability to generate revenues from a product candidate could be postponed, perhaps indefinitely. The resulting negative impact on our operating results and financial condition may cause the value of our common stock to decline, and you may lose all or a part of your investment.

***The approval process outside the United States varies among countries and may limit our ability to develop, manufacture and sell our products internationally. Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad.***

In order to market and sell our products in the European Union and many other jurisdictions, we, and our collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. We may conduct clinical trials for, and seek regulatory approval to market, our product candidates in countries other than the United States. Depending on the results of clinical trials and the process for obtaining regulatory approvals in other countries, we may decide to first seek regulatory approvals of a product candidate in countries other than the U.S., or we may simultaneously seek regulatory approvals in the U.S. and other countries. If we or our collaborators seek marketing approvals for a product candidate outside the U.S., we will be subject to the regulatory requirements of health authorities in each country in which we seek approvals. With respect to marketing authorizations in Europe, we will be required to submit a European marketing authorization application, or MAA, to the European Medicines Agency,

or EMA, which conducts a validation and scientific approval process in evaluating a product for safety and efficacy. The approval procedure varies among regions and countries and can involve additional testing, and the time required to obtain approvals may differ from that required to obtain FDA approval. Obtaining regulatory approvals from health authorities in countries outside the U.S. is likely to subject us to all of the risks associated with obtaining FDA approval described above. In addition, marketing approval by the FDA does not ensure approval by the health authorities of any other country, and approval by foreign health authorities does not ensure marketing approval by the FDA.

***Even if we, or our collaborators, obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.***

Even if we receive regulatory approval for a product candidate, this approval may carry conditions that limit the market for the product or put the product at a competitive disadvantage relative to alternative therapies. For instance, a regulatory approval may limit the indicated uses for which we can market a product or the patient population that may utilize the product, or may be required to carry a warning in its labeling and on its packaging. Products with boxed warnings are subject to more restrictive advertising regulations than products without such warnings. These restrictions could make it more difficult to market any product candidate effectively.

Table of Contents

In addition, manufacturers of approved products and those manufacturers facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, our collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or our collaborators, receive marketing approval for one or more of our product candidates, we, and our collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

***Any of our product candidates for which we, or our collaborators, obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market and we, and our collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our products following approval.***

Any of our product candidates for which we, or our collaborators, obtain marketing approval in the future, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such products, among other things, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the FDA requirement to implement a Risk Evaluation and Mitigation Strategy (REMS) to ensure that the benefits of a drug or biological product outweigh its risks.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers communications regarding off-label use and if we, or our collaborators, do not market any of our product candidates for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing. Violation of the FDCA, the Public Health Service Act (PHSA), and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

***If we do not achieve our projected development and commercialization goals in the timeframes we announce and expect, the commercialization of our product candidates may be delayed, our business will be harmed, and our stock price may decline.***

We sometimes estimate for planning purposes the timing of the accomplishment of various scientific, clinical, regulatory and other product development objectives. These milestones may include our expectations regarding the commencement or completion of scientific studies, clinical trials, the submission of regulatory filings, or commercialization objectives. From time to time, we may publicly announce the expected timing of some of these milestones, such as the completion of an ongoing clinical trial, the initiation of other clinical programs, receipt of

marketing approval, or a commercial launch of a product. The achievement of many of these milestones may be outside of our control. All of these milestones are based on a variety of assumptions which may cause the timing of achievement of the milestones to vary considerably from our estimates, including:

our available capital resources or capital constraints we experience;

the rate of progress, costs and results of our clinical trials and research and development activities, including the extent of scheduling conflicts with participating clinicians and collaborators, and our ability to identify and enroll patients who meet clinical trial eligibility criteria;

our receipt of approvals by the FDA and other regulatory agencies and the timing thereof;

other actions, decisions or rules issued by regulators;

our ability to access sufficient, reliable and affordable supplies of compounds used in the manufacture of our product candidates;

the efforts of our collaborators with respect to the commercialization of our products; and

the securing of, costs related to, and timing issues associated with, product manufacturing as well as sales and marketing activities.

Table of Contents

If we fail to achieve announced milestones in the timeframes we announce and expect, our business and results of operations may be harmed and the price of our stock may decline.

***Our success is dependent in large part upon the continued services of our Chief Scientific Officer.***

Our success is dependent in large part upon the continued services of our Chief Scientific Officer, Dr. David Bar-Or. We have an employment agreement with Dr. Bar-Or and a research agreement with Trauma Research LLC, an entity owned by Dr. Bar-Or that conducts research and development activities on our behalf. These agreements are terminable on short notice for cause by us or Dr. Bar-Or and may also be terminated without cause under certain circumstances. We do not maintain key-man life insurance on Dr. Bar-Or, although we may elect to obtain such coverage in the future. If we lost the services of Dr. Bar-Or for any reason, our clinical testing and other product development activities may experience significant delays, and our ability to develop and commercialize new product candidates may be diminished.

***If we do not obtain the capital necessary to fund our operations, we will be unable to successfully develop, obtain regulatory approval of, and commercialize, pharmaceutical products.***

The development of pharmaceutical products is capital-intensive. At December 31, 2013, we had cash and cash equivalents of approximately $26.3 million. Based upon our current plans, it may be necessary to raise additional capital within the next 12 months. We have not received, and without any form of additional capital financing or revenues do not expect to receive for several years, any revenues from the commercialization of our product candidates. In July 2012 and in September 2013, we obtained a total of approximately $15.4 million and $25.0 million, respectively, in net proceeds from the sale of our common stock in an underwritten public offering and a registered direct offering, respectively. We anticipate we will require significant additional financing to continue to fund our operations beyond the next 12 months. Our future capital requirements will depend on, and could increase significantly as a result of, many factors including:

- progress in, and the costs of, our pre-clinical studies and clinical trials and other research and development programs;
- the scope, prioritization and number of our research and development programs;
- the achievement of milestones or occurrence of other developments that trigger payments under any collaboration agreements we obtain;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the costs involved in filing, prosecuting, enforcing and defending patent claims and other intellectual property rights;
- the costs of securing manufacturing arrangements for commercial production; and

the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory clearances to market our product candidates.

Until we can generate significant continuing revenues, we expect to satisfy our future cash needs through collaboration arrangements, private or public sales of our securities, debt financings, or by licensing one or more of our product candidates. Dislocations in the financial markets have generally made equity and debt financing more difficult to obtain, and may have a material adverse effect on our ability to meet our fundraising needs. We cannot be certain that additional funding will be available to us on acceptable terms, if at all. If funds are not available, we may be required to delay, reduce the scope of, or eliminate one or more of our research or development programs or our commercialization efforts. Additional funding, if obtained, may significantly dilute existing shareholders if that financing is obtained through issuing equity or instruments convertible into equity.

***We rely on third parties to conduct our clinical trials and perform data collection and analysis, which may result in costs and delays that prevent us from successfully commercializing product candidates.***

Although we design and manage our current pre-clinical studies, we do not have the in-house capability to conduct clinical trials for our product candidates. We rely, and will rely in the future, on medical institutions, clinical investigators, contract research organizations, contract laboratories, and collaborators to perform data collection and analysis and other aspects of our clinical trials. We rely primarily on Trauma Research LLC, a related party, to conduct pre-clinical studies and provide assessments of clinical observations.

Our pre-clinical activities or clinical trials conducted in reliance on third parties may be delayed, suspended, or terminated if:

the third parties do not successfully carry out their contractual duties or fail to meet regulatory obligations or expected deadlines;

we replace a third party; or

the quality or accuracy of the data obtained by third parties is compromised due to their failure to adhere to clinical protocols, regulatory requirements, or for other reasons.

Table of Contents

Third party performance failures may increase our development costs, delay our ability to obtain regulatory approval, and delay or prevent the commercialization of our product candidates. While we believe that there are numerous alternative sources to provide these services, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without incurring delays or additional costs.

***Even if collaborators with which we contract in the future successfully complete clinical trials of our product candidates, those candidates may not be commercialized successfully for other reasons.***

Even if we contract with collaborators that successfully complete clinical trials for one or more of our product candidates, those candidates may not be commercialized for other reasons, including:

failure to receive regulatory clearances required to market them as drugs;

being subject to proprietary rights held by others;

being difficult or expensive to manufacture on a commercial scale;

having adverse side effects that make their use less desirable; or

failing to compete effectively with products or treatments commercialized by competitors.

***Relying on third-party manufacturers may result in delays in our clinical trials and product introductions.***

Our core business strategy is to maintain a strong foundation in basic scientific research and combine that foundation with our clinical development capabilities. To date, we have contracted original equipment manufacturers ( OEMs ) to produce the biologic for our Ampion clinical trials and the drug candidate for our Optina clinical trials. Our long-term objective is to build a successful, integrated biopharmaceutical company that provides patients and medical professionals with new and better options for preventing and treating human diseases. However, developing and commercializing new medicines entails significant risks and expenses. We have no manufacturing facilities and have no experience in the manufacturing of drugs or in designing drug-manufacturing processes. We currently obtain the HSA need to produce Ampion for our clinical trials from two manufacturers in the United States. Our clinical trials may be delayed if one or both manufacturers are unable to assure a sufficient quantity of the drug product to meet our study needs. We plan to design, develop and scale up a manufacturing facility in Denver, Colorado where we would manufacture Ampion for registration, batching and commercial supply, as well as future clinical supplies. If we experience delays or difficulties in this effort, our clinical trials may be impacted, our commercialization efforts may be impeded, or our costs may increase. We obtain the active pharmaceutical ingredient ( API ) for Optina from an Indian company, which is one of only four suppliers of the API in the world. Our clinical trials and ultimately FDA approval may be delayed if we are unable to obtain a sufficient quantity of the drug product on a timely basis or if we need to establish an alternative source of supply for the API.

Once regulatory approval is obtained, a marketed product and its manufacturer are subject to continual review. The discovery of previously unknown problems with a product or manufacturer may result in restrictions on the product, manufacturer or manufacturing facility, including withdrawal of the product from the market. Any manufacturers with

which we contract HSA for Ampion or danazol for Optina supplies are required to operate in accordance with FDA-mandated current good manufacturing practices, or cGMPs. A failure of any of our contract manufacturers to establish and follow cGMPs and to document their adherence to such practices may lead to significant delays in the launch of products based on our product candidates into the market. Failure by third-party manufacturers to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, revocation or suspension of marketing approval for any products granted pre-market approvals, seizures or recalls of products, operating restrictions, and criminal prosecutions.

***Our transactions with related parties may not benefit us and may harm us.***

We are party to a sponsored research agreement with Trauma Research LLC, a related party controlled by our director and Chief Scientific Officer, Dr. Bar-Or. We rely primarily on Trauma Research LLC to conduct pre-clinical studies and provide assessments of clinical observations. In addition, Luoxis is party to an agreement with Trauma Research LLC, under which Luoxis pays Trauma Research LLC for services related to research and development of Luoxis Oxidation-Reduction Potential platform.

We believe that we have conducted our related-party transactions on an arm s-length basis and on terms comparable to, or more favorable to us than, similar transactions we would enter into with independent third parties. However, we cannot assure you that all our future transactions with related parties will be beneficial to us.

***We intend to enter into agreements with third parties to sell and market any products we develop and for which we obtain regulatory approvals, which may affect the sales of our products and our ability to generate revenues.***

Table of Contents

We do not currently maintain an organization for the sale, marketing and distribution of pharmaceutical products and may contract with, or license, third parties to market any products we develop that receive regulatory approvals. Outsourcing sales and marketing in this manner may subject us to a variety of risks, including:

- our inability to exercise control over sales and marketing activities and personnel;
- failure or inability of contracted sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe our products;
- disputes with third parties concerning sales and marketing expenses, calculation of royalties, and sales and marketing strategies; and
- unforeseen costs and expenses associated with sales and marketing.

If we are unable to partner with a third party that has adequate sales, marketing, and distribution capabilities, we may have difficulty commercializing our product candidates, which would adversely affect our business, financial condition, and ability to generate product revenues.

***We face substantial competition from companies with considerably more resources and experience than we have, which may result in others discovering, developing, receiving approval for, or commercializing products before or more successfully than us.***

Our ability to succeed in the future depends on our ability to discover, develop and commercialize pharmaceutical products that offer superior efficacy, convenience, tolerability, and safety when compared to existing treatment methodologies. We intend to do so by identifying product candidates that address new indications using previously approved drugs, use of new combinations of previously approved drugs, or which are based on a modified active ingredient which previously received regulatory approval. Because our strategy is to develop new product candidates primarily for treatment of diseases that affect large patient populations, those candidates are likely to compete with a number of existing medicines or treatments, and a large number of product candidates that are being developed by others.

Many of our potential competitors have substantially greater financial, technical, personnel and marketing resources than we do. In addition, many of these competitors have significantly greater resources devoted to product development and pre-clinical research. Our ability to compete successfully will depend largely on our ability to:

- discover and develop product candidates that are superior to other products in the market;
- attract and retain qualified personnel;
- obtain patent and/or other proprietary protection for our product candidates;

obtain required regulatory approvals; and

obtain collaboration arrangements to commercialize our product candidates.

Established pharmaceutical companies devote significant financial resources to discovering, developing or licensing novel compounds that could make our product candidates obsolete. Our competitors may obtain patent protection, receive FDA approval, and commercialize medicines before us. Other companies are engaged in the discovery of compounds that may compete with the product candidates we are developing.

Any new product that competes with a currently-approved treatment or medicine must demonstrate compelling advantages in efficacy, convenience, tolerability and/or safety in order to address price competition and be commercially successful. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

***Product liability and other lawsuits could divert our resources, result in substantial liabilities and reduce the commercial potential of our product candidates.***

The risk that we may be sued on product liability claims is inherent in the development and commercialization of pharmaceutical products. Side effects of, or manufacturing defects in, products that we develop which are commercialized by any collaborators could result in the deterioration of a patient s condition, injury or even death. Once a product is approved for sale and commercialized, the likelihood of product liability lawsuits increases. Claims may be brought by individuals seeking relief for themselves or by individuals or groups seeking to represent a class. These lawsuits may divert our management from pursuing our business strategy and may be costly to defend. In addition, if we are held liable in any of these lawsuits, we may incur substantial liabilities and may be forced to limit or forgo further commercialization of the affected products.

We may be subject to legal or administrative proceedings and litigation other than product liability lawsuits which may be costly to defend and could materially harm our business, financial conditions and operations.

Table of Contents

Although we maintain general liability and product liability insurance, this insurance may not fully cover potential liabilities. In addition, inability to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product or other legal or administrative liability claims could prevent or inhibit the commercial production and sale of any of our product candidates that receive regulatory approval, which could adversely affect our business. Product liability claims could also harm our reputation, which may adversely affect our collaborators ability to commercialize our products successfully.

***If any of our product candidates are commercialized, this does not assure acceptance by physicians, patients, third party payors, or the medical community in general. Even if we, or our collaborators, are able to commercialize our product candidates, the products may become subject to unfavorable pricing regulations, third party payor reimbursement practices or healthcare reform initiatives that could harm our business.***

The commercial success of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third party payors. If reimbursement is not available, or is available only to limited levels, we, or our collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or our collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. We cannot be sure that any of our product candidates, if and when approved for marketing, will be accepted by these parties. Even if the medical community accepts a product as safe and efficacious for its indicated use, physicians may choose to restrict the use of the product if we or any collaborator is unable to demonstrate that, based on experience, clinical data, side-effect profiles and other factors, our product is preferable to any existing medicines or treatments. We cannot predict the degree of market acceptance of any product candidate that receives marketing approval, which will depend on a number of factors, including, but not limited to:

- the demonstration of the clinical efficacy and safety of the product;
- the approved labeling for the product and any required warnings;
- the advantages and disadvantages of the product compared to alternative treatments;
- our and any collaborator s ability to educate the medical community about the safety and effectiveness of the product;
- the reimbursement policies of government and third party payors pertaining to the product; and
- the market price of our product relative to competing treatments.

***Government restrictions on pricing and reimbursement, as well as other healthcare payor cost-containment initiatives, may negatively impact our ability to generate revenues if we obtain regulatory approval to market a product.***

The continuing efforts of the government, insurance companies, managed care organizations and other payors of health care costs to contain or reduce costs of health care may adversely affect one or more of the following:

- our or our collaborators ability to set a price we believe is fair for our products, if approved;
- our ability to generate revenues and achieve profitability; and
- the availability of capital.

The 2010 enactments of the Patient Protection and Affordable Care Act, or PPACA, and the Health Care and Education Reconciliation Act are expected to significantly impact the provision of, and payment for, health care in the United States. Various provisions of these laws take effect over the next four years, and are designed to expand Medicaid eligibility, subsidize insurance premiums, provide incentives for businesses to provide health care benefits, prohibit denials of coverage due to pre-existing conditions, establish health insurance exchanges, and provide additional support for medical research. Additional legislative proposals to reform healthcare and government insurance programs, along with the trend toward managed healthcare in the United States, could influence the purchase of medicines and reduce demand and prices for our products, if approved. This could harm our or our collaborators ability to market any products and generate revenues. Cost containment measures that health care payors and providers are instituting and the effect of further health care reform could significantly reduce potential revenues from the sale of any of our product candidates approved in the future, and could cause an increase in our compliance, manufacturing, or other operating expenses. In addition, in certain foreign markets, the pricing of prescription drugs is subject to government control and reimbursement may in some cases be unavailable. We believe that pricing pressures at the federal and state level, as well as internationally, will continue and may increase, which may make it difficult for us to sell our potential products that may be approved in the future at a price acceptable to us or any of our future collaborators.

***If Trauma Research LLC uses hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages or fines.***

Table of Contents

The research and development activities conducted on our behalf by Trauma Research LLC, a related party controlled by Dr. Bar-Or, involve the controlled use of potentially hazardous substances, including chemical, biological and radioactive materials. In addition, Trauma Research LLC s operations produce hazardous waste products. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. If Trauma Research LLC experiences a release of hazardous substances, it is possible that this release could cause personal injury or death, and require decontamination of facilities. Trauma Research LLC has advised us that it believes it is in compliance with laws applicable to the handling of hazardous substances, but such compliance does not assure that a release of hazardous substances will not occur, or assure that such compliance will be maintained in the future. In the event of an accident involving research being conducted on our behalf, Trauma Research LLC could be held liable for damages or face substantial penalties for which we could also be responsible. We do not have any insurance for liabilities arising from the procurement, handling, or discharge of hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business.

***Business interruptions could limit our ability to operate our business.***

Our operations are vulnerable to damage or interruption from computer viruses, human error, natural disasters, telecommunications failures, intentional acts of misappropriation, and similar events. We have not established a formal disaster recovery plan, and our back-up operations and our business interruption insurance may not be adequate to compensate us for losses that occur. A significant business interruption could result in losses or damages incurred by us and require us to curtail our operations.

**Risks Related to Our Intellectual Property**

***Our ability to compete may decline if we do not adequately protect our proprietary rights.***

Our commercial success depends on obtaining and maintaining proprietary rights to our product candidates and compounds and their uses, as well as successfully defending these rights against third-party challenges. We will only be able to protect our product candidates, proprietary compounds, and their uses from unauthorized use by third parties to the extent that valid and enforceable patents, or effectively protected trade secrets, cover them.

Our ability to obtain patent protection for our product candidates and compounds is uncertain due to a number of factors, including:

- we may not have been the first to make the inventions covered by pending patent applications or issued patents;
- we may not have been the first to file patent applications for our product candidates or the compounds we developed or for their uses;
- others may independently develop identical, similar or alternative products or compounds;

our disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability;

any or all of our pending patent applications may not result in issued patents;

we may not seek or obtain patent protection in countries that may eventually provide us a significant business opportunity;

any patents issued to us may not provide a basis for commercially viable products, may not provide any competitive advantages, or may be successfully challenged by third parties;

our proprietary compounds may not be patentable;

others may design around our patent claims to produce competitive products which fall outside of the scope of our patents; or

others may identify prior art which could invalidate our patents.

Even if we have or obtain patents covering our product candidates or compounds, we may still be barred from making, using and selling our product candidates or technologies because of the patent rights of others. Others have or may have filed, and in the future may file, patent applications covering compounds or products that are similar or identical to ours. There are many issued U.S. and foreign patents relating to chemical compounds and therapeutic products, and some of these relate to compounds we intend to commercialize. Numerous U.S. and foreign issued patents and pending patent applications owned by others exist in the area of metabolic disorders, cancer, inflammatory responses, and the other fields in which we are developing products. These could materially affect our ability to develop our product candidates or sell our products if approved. Because patent applications can take many years to issue, there may be currently pending applications unknown to us that may later result in issued patents that our product candidates or compounds may infringe. These patent applications may have priority over patent applications filed by us.

We periodically conduct searches to identify patents or patent applications that may prevent us from obtaining patent protection for our compounds or that could limit the rights we have claimed in our patents and patent applications. Disputes may arise regarding the source or ownership of our inventions. It is difficult to determine if and how such disputes would be resolved. Others may challenge

Table of Contents

the validity of our patents. If our patents are found to be invalid, we will lose the ability to exclude others from making, using or selling the compounds or products addressed in those patents. In addition, compounds or products we may license may become important to some aspects of our business. We generally will not control the prosecution, maintenance or enforcement of patents covering licensed compounds or products.

***Confidentiality agreements with employees and others may not adequately prevent disclosure of our trade secrets and other proprietary information and may not adequately protect our intellectual property, which could limit our ability to compete.***

Because we operate in the highly technical field of drug discovery and development of therapies that can address metabolic disorders, cancer, inflammation and other conditions, we rely in part on trade secret protection in order to protect our proprietary technology and processes. However, trade secrets are difficult to protect. We enter into confidentiality and intellectual property assignment agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party or made known to the party by us during the course of the party s relationship with us. These agreements also generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property.

However, these agreements may not be honored and may not effectively assign intellectual property rights to us. Enforcing a claim that a party illegally obtained and is using our trade secrets is difficult, expensive and time consuming and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets. The failure to obtain or maintain trade secret protection could adversely affect our competitive position. We have entered into non-compete agreements with certain of our employees, but the enforceability of those agreements is not assured.

***A dispute concerning the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be time consuming and costly, and an unfavorable outcome could harm our business.***

There is significant litigation in the pharmaceutical industry regarding patent and other intellectual property rights. While we are not currently subject to any pending intellectual property litigation, and are not aware of any such threatened litigation, we may be exposed to future litigation by third parties based on claims that our product candidates, technologies or activities infringe the intellectual property rights of others. In particular, there are many patents relating to repositioned drugs and chemical compounds used to treat metabolic disorders, cancer and inflammation. Some of these may encompass repositioned drugs or compounds that we utilize in our product candidates. If our development activities are found to infringe any such patents, we may have to pay significant damages or seek licenses to such patents. A patentee could prevent us from using the patented drugs or compounds. We may need to resort to litigation to enforce a patent issued to us, to protect our trade secrets, or to determine the scope and validity of third-party proprietary rights. From time to time, we may hire scientific personnel or consultants formerly employed by other companies involved in one or more areas similar to the activities conducted by us. Either we or these individuals may be subject to allegations of trade secret misappropriation or other similar claims as a result of prior affiliations. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources, regardless of whether we win or lose. We may not be able to afford the costs of litigation. Any legal action against us or our collaborators could lead to:

- payment of damages, potentially treble damages, if we are found to have willfully infringed a party s patent rights;

injunctive or other equitable relief that may effectively block our ability to further develop, commercialize, and sell products; or

us or our collaborators having to enter into license arrangements that may not be available on commercially acceptable terms, if at all.

As a result, we could be prevented from commercializing current or future product candidates.

***Pharmaceutical patents and patent applications involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our patent position.***

The patent positions of pharmaceutical companies can be highly uncertain and involve complex legal and factual questions. For example, some of our patents and patent applications cover methods of use of repositioned drugs, while other patents and patent applications cover composition of a particular compound. The interpretation and breadth of claims allowed in some patents covering pharmaceutical compounds may be uncertain and difficult to determine, and are often affected materially by the facts and circumstances that pertain to the patented compound and the related patent claims. The standards of the United States Patent and Trademark Office, or USPTO, are sometimes uncertain and could change in the future. Consequently, the issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, and U.S. patents may be subject to reexamination proceedings in the USPTO. Foreign patents may be subject also to opposition or comparable proceedings in the corresponding foreign patent office, which could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such interference, reexamination and opposition proceedings may be costly. Accordingly, rights under any issued patents may not provide us with sufficient protection against competitive products or processes.

Table of Contents

In addition, changes in or different interpretations of patent laws in the United States and foreign countries may permit others to use our discoveries or to develop and commercialize our technology and products without providing any compensation to us, or may limit the number of patents or claims we can obtain. The laws of some countries do not protect intellectual property rights to the same extent as U.S. laws and those countries may lack adequate rules and procedures for defending our intellectual property rights. For example, some countries do not grant patent claims directed to methods of treating humans and, in these countries, patent protection may not be available at all to protect our product candidates. In addition, U.S. patent laws may change, which could prevent or limit us from filing patent applications or patent claims to protect our products and/or compounds.

If we fail to obtain and maintain patent protection and trade secret protection of our product candidates, proprietary compounds and their uses, we could lose our competitive advantage and competition we face would increase, reducing any potential revenues and adversely affecting our ability to attain or maintain profitability.

**Risks Related to Our Common Stock**

***The price of our stock has been extremely volatile and may continue to be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.***

The price of our common stock has been extremely volatile and may continue to be so. The stock market in general and the market for pharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies, to a greater extent during the last few years. The following factors, in addition to the other risk factors described in this section, may also have a significant impact on the market price of our common stock:

- any actual or perceived adverse developments in clinical trials for Ampion, Optina or the ORP device;
- any actual or perceived difficulties or delays in obtaining regulatory approval of any of our product candidates in the United States or other countries once clinical trials are completed;
- any finding that our product candidates are not safe or effective, or any inability to demonstrate clinical effectiveness of our product candidates when compared to existing treatments;
- any actual or perceived adverse developments in repurposed drug technologies, including any change in FDA policy or guidance on approval of repurposed drug technologies for new indications;
- any announcements of developments with, or comments by, the FDA, the EMA, or other regulatory authorities with respect to product candidates we have under development;
- any announcements concerning our retention or loss of key employees, especially Dr. Bar-Or;

our success or inability to obtain collaborators to conduct clinical trials, commercialize a product candidate for which regulatory approval is obtained, or market and sell an approved product candidate;

any actual or perceived adverse developments with respect to our relationship with Trauma Research LLC;

any licensee s termination of a license, such as that experienced with Zertane in 2010;

announcements of patent issuances or denials, product innovations, or introduction of new commercial products by our competitors that will compete with any of our product candidates;

publicity regarding actual or potential study results or the outcome of regulatory reviews relating to products under development by us, our collaborators, or our competitors;

economic and other external factors beyond our control; and

sales of stock by us or by our shareholders.

In addition, we believe there has been and may continue to be substantial off-market transactions in derivatives of our stock, including short selling activity or related similar activities, which are beyond our control and which may be beyond the full control of the SEC and Financial Institutions Regulatory Authority ( FINRA ). While SEC and FINRA rules prohibit some forms of short selling and other activities that may result in stock price manipulation, such activity may nonetheless occur without detection or enforcement. We have held conversations with regulators concerning trading activity in our stock; however, there can be no assurance that should there be any illegal manipulation in the trading of our stock it will be detected, prosecuted or successfully eradicated. Significant short selling or other types of market manipulation could cause our stock trading price to decline, to become more volatile, or both.

Table of Contents

***The price of our stock may be vulnerable to manipulation.***

In December 2011, our common stock was the subject of significant short selling efforts by certain market participants. Short sales are transactions in which a market participant sells a security that it does not own. To complete the transaction, the market participant must borrow the security to make delivery to the buyer. The market participant is then obligated to replace the security borrowed by purchasing the security at the market price at the time of required replacement. If the price at the time of replacement is lower than the price at which the security was originally sold by the market participant, then the market participant will realize a gain on the transaction. Thus, it is in the market participant s interest for the market price of the underlying security to decline as much as possible during the period prior to the time of replacement.

Because our unrestricted public float (not subject to lockup restrictions) has been small relative to other issuers, previous short selling efforts have impacted, and may in the future continue to impact, the value of our stock in an extreme and volatile manner to our detriment and the detriment of our shareholders. In addition, market participants with admitted short positions in our stock have published, and may in the future continue to publish, negative information regarding us and our management team on internet sites or blogs that we believe is inaccurate and misleading. We believe that the publication of this negative information has led, and may in the future continue to lead, to significant downward pressure on the price of our stock to our detriment and the further detriment of our shareholders. These and other efforts by certain market participants to manipulate the price of our common stock for their personal financial gain may cause our stockholders to lose a portion of their investment, may make it more difficult for us to raise equity capital when needed without significantly diluting existing stockholders, and may reduce demand from new investors to purchase shares of our stock.

***If we cannot continue to satisfy the NYSE MKT listing maintenance requirements and other rules, including the director independence requirements, our securities may be delisted, which could negatively impact the price of our securities.***

Although our common stock is listed on the NYSE MKT, we may be unable to continue to satisfy the listing maintenance requirements and rules. If we are unable to satisfy the NYSE MKT criteria for maintaining our listing, our securities could be subject to delisting. To qualify for continued listing on the NYSE MKT, we must continue to meet specific criteria, including the following:

The minimum bid price of our shares must be at least $3.00, the market value of our publicly held shares must be at least $15,000,000, our stockholders equity must be at least $4,000,000, and we must have at least (i) 800 public shareholders and 500,000 publicly held shares, or; (ii) 400 public shareholders and 1,000,000 publicly held shares; or

The minimum bid price of our shares must be at least $2.00, the market value of our publicly held shares must be at least $15,000,000, our stockholders equity must be at least $4,000,000, our market capitalization must exceed $50,000,000, and we must have at least (i) 800 public shareholders and 500,000 publicly held shares, or; (ii) 400 public shareholders and 1,000,000 publicly held shares; or

The minimum bid price of our shares must be at least $3.00, the market value of our publicly held shares must be at least $20,000,000, our market capitalization must exceed $75,000,000 or our assets and revenue

must exceed $75,000,000, and we must have at least (i) 800 public shareholders and 500,000 publicly held shares, or; (ii) 400 public shareholders and 1,000,000 publicly held shares.

Under the NYSE MKT rules, shares that are held by public shareholders do not include shares held by officers, directors, controlling shareholders and concentrated (10% or greater), affiliated or family holdings.

If the NYSE MKT delists our securities, we could face significant consequences, including:

a limited availability for market quotations for our securities;

reduced liquidity with respect to our securities;

a determination that our common stock is a penny stock, which will require brokers trading in our common stock to adhere to more stringent rules and possibly result in reduced trading;

activity in the secondary trading market for our common stock;

limited amount of news and analyst coverage; and

a decreased ability to issue additional securities or obtain additional financing in the future.

In addition, we would no longer be subject to the NYSE MKT rules, including rules requiring us to have a certain number of independent directors and to meet other corporate governance standards.

Table of Contents

***Concentration of our ownership limits the ability of our shareholders to influence corporate matters.***

As of December 31, 2013, our directors, executive officers and their affiliates beneficially owned approximately 13.7% of our outstanding common stock. These shareholders may control effectively the outcome of actions taken by us that require shareholder approval.

***Anti-takeover provisions in our charter and bylaws and in Delaware law could prevent or delay a change in control of Ampio.***

Provisions of our certificate of incorporation and bylaws may discourage, delay or prevent a merger or acquisition that shareholders may consider favorable, including transactions in which shareholders might otherwise receive a premium for their shares. These provisions include:

- requiring supermajority shareholder voting to effect certain amendments to our certificate of incorporation and bylaws;
- restricting the ability of shareholders to call special meetings of shareholders;
- prohibiting shareholder action by written consent except in certain circumstances; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on by shareholders at shareholder meetings.

***Increased costs associated with corporate governance compliance may significantly impact our results of operations.***

Changing laws, regulations and standards relating to corporate governance, public disclosure and compliance practices, including the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the Sarbanes-Oxley Act of 2002, and new SEC regulations, may create difficulties for companies such as ours in understanding and complying with these laws and regulations. As a result of these difficulties and other factors, devoting the necessary resources to comply with evolving corporate governance and public disclosure standards has resulted in and may in the future result in increased general and administrative expenses and a diversion of management time and attention to compliance activities. We also expect these developments to increase our legal compliance and financial reporting costs. In addition, these developments may make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. Moreover, we may be unable to comply with these new laws and regulations on a timely basis.

These developments could make it more difficult for us to retain qualified members of our Board of Directors, or qualified executive officers. We are presently evaluating and monitoring regulatory developments and cannot estimate the timing or magnitude of additional costs we may incur as a result. To the extent these costs are significant; our general and administrative expenses are likely to increase.

***If securities analysts do not publish research or reports about our business or if they downgrade our stock after instituting coverage, the price of our common stock could decline.***

The research and reports that industry or financial analysts publish about us or our business may vary widely and may not predict accurate results, but will likely have an effect on the trading price of our common stock. If an industry analyst decides not to cover us, or if an industry analyst institutes coverage and later decides to cease covering us, we could lose visibility in the market, which in turn could cause our stock price to decline. If an industry analyst who covers our stock decides to downgrade that stock, our stock price would likely decline rapidly in response.

***We have no plans to pay dividends on our common stock.***

We have no plans to pay dividends on our common stock. We generally intend to invest future earnings, if any, to fund our growth. Any payment of future dividends will be at the discretion of our Board of Directors and will depend on, among other things, our earnings, financial condition, capital requirements, level of indebtedness, statutory and contractual restrictions applying to the payment of dividends and other considerations our Board of Directors deem relevant. Any future credit facilities or preferred stock financing we obtain may further limit our ability to pay dividends on our common stock.

**Item 1B.** ***Unresolved Staff Comments***

None.

**Item 2.** ***Properties***

We maintain our headquarters in leased space in Greenwood Village, Colorado, for a monthly rental of approximately $8,900. The lease expires in July 2014. We anticipate that the lease can be renewed on terms similar to those now in effect.

On December 16, 2013, we announced a ten-year lease of a multi-purpose facility in the Denver Metro Area containing 19,346 square feet. This facility will include an FDA compliant clean room to manufacture Ampion and will be our new headquarters. The facility is expected to be operational by the summer of 2014.

Table of Contents

**Item 3.** ***Legal Proceedings***

On August 30, 2013, Ampio was notified of a civil complaint filed against the Company and certain of its directors and executive officers as defendants. The Complaint alleges that the defendants breached a contract with the plaintiffs for consulting services the plaintiffs purportedly provided during two time periods: in November and December 2009 in connection with a proposed reverse merger transaction, and between 2010 and 2012. The reverse merger transaction identified by the plaintiffs, and which is alleged to be the basis for contract claims, was not consummated by the Company. The plaintiffs seek an unspecified amount of compensatory damages and other relief, including 1,130,000 shares of the Company s common stock, and also assert claims for promissory estoppel, unjust enrichment and fraudulent inducement and concealment. The Company believes these claims are without merit and intends to defend this lawsuit vigorously.

In addition, from time to time we may be subject to other legal proceedings, claims, and litigation arising in the ordinary course of business. We do not, however, currently expect that the ultimate costs to resolve any pending matter will have a material effect on our consolidated financial position, results of operations, or cash flows.

**Item 4.** ***Mine Safety Disclosures.***

Not applicable.

Table of Contents

## PART II

### Item 5. *Market for Registrant s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities*

**Market Data**

On June 17, 2013, our common stock began trading on the NYSE MKT under the ticker symbol AMPE . It was previously quoted on the NASDAQ Capital Market under the same ticker symbol AMPE . Before it was listed on the NASDAQ Capital Market exchange, it was previously quoted on the Over-the-Counter Bulletin Board under the symbol AMPE.OB. The following table sets forth the high and low last reported sale price information for our common stock for each quarter for the past three fiscal years.

| | Common Stock | |
|---|---|---|
| | High | Low |
| First quarter 2011 | $ 8.75 | $ 2.20 |
| Second quarter 2011 | $ 8.61 | $ 2.80 |
| Third quarter 2011 | $ 9.19 | $ 4.32 |
| Fourth quarter 2011 | $ 8.26 | $ 3.77 |
| First quarter 2012 | $ 4.51 | $ 2.68 |
| Second quarter 2012 | $ 5.08 | $ 2.56 |
| Third quarter 2012 | $ 5.43 | $ 2.65 |
| Fourth quarter 2012 | $ 4.12 | $ 3.14 |
| First quarter 2013 | $ 4.89 | $ 3.65 |
| Second quarter 2013 | $ 6.72 | $ 4.63 |
| Third quarter 2013 | $ 7.79 | $ 5.27 |
| Fourth quarter 2013 | $ 10.55 | $ 6.62 |

As of February 4, 2014, there were of record approximately 5,400 holders of our common stock.

We have never paid cash dividends and intend to employ all available funds in the development of our business. We have no plans to pay cash dividends in the near future. If we issue in the future any preferred stock or obtain financing from a bank, the terms of those financings may contain restrictions on our ability to pay dividends for so long as the preferred stock or bank financing is outstanding.

**Performance Graph**

We have presented below the cumulative return to our stockholders during the period from January 1, 2011 through December 31, 2013 in comparison to the cumulative return NASDAQ Biotechnology Index and the Russell 2000 Index. The comparisons are based on historical data and are not indicative of, nor intended to forecast, the future performance of our common stock.

Table of Contents

The information under Performance Graph is not deemed to be soliciting material or filed with the Securities and Exchange Commission or subject to Regulation 14A or 14C, or to the liabilities of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference in any filing of Ampio Pharmaceuticals, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K and irrespective of any general incorporation language in those filings.

**Unregistered Sales of Equity Securities and Use of Proceeds**

Information regarding unregistered sales of equity securities and use of proceeds is incorporated by reference to Item 15 of Part IV, Notes to Consolidated Financial Statements Note 7 Short Term Debt and Note 12 Common Stock of this annual report on Form 10K.

**Equity Compensation Plan Information**

At the special meeting on March 1, 2010, our shareholders approved the adoption of a stock and option award plan (the 2010 Plan ), under which 2,500,000 shares were reserved for future issuance under restricted stock awards, options, and other equity awards. The 2010 Plan permits grants of equity awards to employees, directors and consultants. On August 15, 2010, the number of shares issuable under the 2010 Plan was increased to 4,500,000 shares by consent of our majority shareholders. At the annual shareholders meeting, held December 3, 2011, the number of shares issuable under the 2010 Plan was increased to 5,700,000. At the annual shareholders meeting held December 15, 2012, the number of shares issuable under the 2010 Plan was further increased to 8,200,000 and, recently, on December 14, 2013, total shares issuable was increased to 11,700,000. The following table displays equity compensation plan information as of December 31, 2013.

| Plan Category | Number of Securities to be Issued upon Exercise of Outstanding Options, Warrants and Rights (a) | Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights (b) | Number of Securities Remaining Available for Issuance under Equity Compensation Plans (Excluding Securities Reflected in Column (a)) (c) |
|---|---|---|---|
| Equity compensation plans approved by security holders | 5,135,058 | $ 3.54 | 5,313,689 |
| Equity compensation plans not approved by security holders | | | |
| Total | 5,135,058 | $ 3.54 | 5,313,689 |

Table of Contents

**Item 6.** ***Selected Financial Data***

Our selected consolidated financial data shown below should be read together with Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations and our consolidated financial statements and respective notes included in Item 8 Financial Statements and Supplementary Data referencing Item 15 of Part IV. The data shown below is not necessarily indicative of results to be expected for any future period.

| | Years Ended December 31, | | | | |
|---|---|---|---|---|---|
| | 2013 | 2012 | 2011 | 2010 | 2009 |
| **Selected Statements of Operations Data:** | | | | | |
| License revenue | $ 50,000 | $ 50,000 | $ 18,750 | $ | $ |
| Research and development | 18,288,871 | 7,493,824 | 6,648,397 | 1,972,134 | 1,070,370 |
| General and administrative | 5,785,002 | 4,376,932 | 4,504,494 | 4,732,271 | 441,135 |
| Interest income (expense) | 12,287 | 21,943 | (1,674) | (18,730) | (323) |
| Unrealized gain (loss) on fair value of debt instruments | | | (5,585,422) | 37,511 | |
| Derivative income (expense) | (516,840) | 205,768 | (1,555,497) | (1,367,771) | |
| Net loss, before income tax | (24,528,426) | (11,593,045) | (18,276,734) | (8,053,395) | (1,511,828) |
| Foreign tax expense | | | 82,500 | | |
| Net loss applicable to non-controlling interests | 519,868 | | | | |
| Net loss applicable to Ampio | $ (24,008,558) | $ (11,593,045) | $ (18,359,234) | $ (8,053,395) | $ (1,511,828) |
| **Per share data:** | | | | | |
| Weighted average number of Ampio common shares outstanding | 38,294,259 | 33,983,590 | 26,013,838 | 16,288,468 | 14,793,068 |
| Basic and diluted Ampio net loss per common share | $ (0.63) | $ (0.34) | $ (0.71) | $ (0.49) | $ (0.10) |
| **Selected Balance Sheets Data:** | | | | | |
| Cash and cash equivalents | $ 26,309,449 | $ 17,682,517 | $ 11,362,325 | $ 671,279 | $ 71,983 |
| Fixed assets, net | 1,298,504 | 59,290 | 76,230 | | |
| In-process research and development | 7,500,000 | 7,500,000 | 7,500,000 | | |
| Patents, net | 734,957 | 420,468 | 465,924 | | |
| Total assets | 36,018,752 | 25,847,165 | 19,482,599 | 737,524 | 86,280 |
| Accounts payable | 1,900,576 | 1,201,122 | 630,622 | 464,453 | 79,445 |
| Accrued wages and other liabilities | 522,056 | | | 526,733 | 73,391 |
| Senior convertible unsecured related party debentures | | | | 608,846 | |
| Senior unsecured manditorily convertible debentures | | | | 2,133,743 | |
| Warrant derivative liability | | 384,771 | 610,911 | 398,671 | |
| Long-term deferred revenue | 331,250 | 381,250 | 431,250 | | |

| | | | | | |
|---|---|---|---|---|---|
| Total liabilities | 2,803,882 | 2,017,143 | 1,722,783 | 4,745,960 | 354,250 |
| Total Ampio stockholders equity (deficit) | 33,214,870 | 23,830,022 | 17,759,816 | (4,008,436) | (267,970) |

Table of Contents

**Item 7.** ***Management s Discussion and Analysis of Financial Condition and Results of Operations***

*You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes appearing elsewhere in this report. Some of the information contained in this discussion and analysis, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should read the Risk Factors section of this Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.*

**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 are also focused on developing and monetizing our ORP diagnostic device and sexual dysfunction portfolio.

***Dose Ranging SPRING Pivotal 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, from baseline for Ampion compared to the same volume of saline. Secondary endpoints included evaluating safety and disease severity, as well as stiffness and function. Both Ampion dose cohorts experienced statistically significant reductions in pain compared to control, and there were no significant differences between the efficacy of the two Ampion doses. 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 -0.25 (95% CI: -0.41 to -0.08, p = 0.004).

Patients receiving Ampion experienced, on average, a greater than 40% reduction in pain from baseline.

Patients receiving Ampion achieved significantly greater reduction in pain, WOMAC A, across 12 weeks compared to saline vehicle control (p = 0.01)

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 Patient Global Assessment ( PGA ) of disease severity 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).

Severe patients, defined as Kellgren-Lawrence IV, receiving Ampion achieved significantly greater reduction in pain, WOMAC A, from baseline to 12 weeks compared to severe patients receiving saline vehicle control (p = 0.017)

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 ).

On February 4, 2014, we announced that an article reporting the results of the SPRING study was published in PLOSE ONE, an international, open-access, online publication. The article entitled: A Randomized Clinical Trial to Evaluate Two Doses of an Intra-Articular Injection of LMWF-5A in Adults with Pain Due to Osteoarthritis of the Knee details the efficacy and safety outcomes of the use of Ampion in the SPRING study.

We decided to follow 97 patients who were administered either 4 mL Ampion or saline vehicle control for an additional 8 weeks past the original 12 week primary endpoint. At week twenty, 50% of patients in the Kellgren-Lawrence grades of 3 and 4 (severe osteoarthritis) had improvement of 40% or more in the WOMAC A pain scale compared to 25% in the vehicle control group (p=0.04). Patients were also classified as responders if they achieved 40% or greater improvement in pain, WOMAC A, and function, WOMAC C, at and over 20 weeks after a single intra-articular injection into the knee. In these same grade 3 & 4 patients, there was a

Table of Contents

statistically significant improvement in pain, WOMAC A, compared to the vehicle control both at week 20 (p=0.02) and over the whole period of 20 weeks (p=0.005). Also in these same grade 3 & 4 patients, there was a statistically significant improvement in function, WOMAC C, compared to vehicle control both at week 20 (p=0.05) and over the whole period of 20 weeks (p=0.04).

***Ongoing US Clinical Trials***

On January 13, 2014, we announced the first patient injection in the Phase III final pivotal clinical trial of Ampion for the treatment of osteoarthritis of the knee. The Phase III STEP study has been designed to enroll 500 patients and the primary endpoint is reduction in pain for patients treated with Ampion compared to vehicle control at 12 weeks. STEP is a randomized, placebo-controlled, double-blind study in which patients with osteoarthritis knee pain will be randomized to receive either a 4 mL single injection of Ampion or saline control. The clinical effects of treatment on osteoarthritic pain will be evaluated during clinic visits at 6, 12, and 20 weeks using WOMAC Osteoarthritis Index and the PGA of disease severity. Safety will be assessed by recording adverse events, concomitant medications, physical examination, vital signs and clinical laboratory tests. Topline results are anticipated in the third quarter of 2014.

We commenced enrollment in a 450 patient Phase IIb trial in February 2013 of Optina for the treatment of DME. 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 300 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 (0.5 mg per BMI and 1.0 mg 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. 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 was determined by an interim analysis occurring at week 4 involving approximately 150 patients.

**Recent Financing Activities**

On September 30, 2011 Ampio filed a shelf registration statement on Form S-3 with the Securities and Exchange Commission ( SEC ) to register Ampio common stock and warrants in an aggregate amount of up to $80 million for offering from time to time in the future. The shelf registration was declared effective on October 28, 2011 by the SEC. Of the $80 million in Ampio common stock registered under the shelf, $28.4 remains under such registration statement after the sales referenced below.

On December 26, 2013, Ampio filed an additional shelf registration statement on Form S-3 with the SEC to register Ampio common stock and warrants in an aggregate amount of up to $100 million for offering from time to time in the future. The registration statement also registers for possible resale up to 1,500,000 shares of common stock to be sold by directors and management (as selling shareholders) in future public offerings. The shelf registration was declared effective on January 22, 2014 by the Securities and Exchange Commission.

In January 2013, we formed a subsidiary, Luoxis Diagnostics, Inc. ( Luoxis ) to focus on the development and commercialization of our Oxidation Reduction Potential ( ORP ) technology platform. Luoxis was funded through a private placement which had a final closing on May 31, 2013 with $4,652,000 in gross proceeds. Net proceeds were

$3,980,290 after placement agent and legal fees. Prior to the private placement, Ampio incurred all of the costs associated with the development of the ORP platform. As a result of the private placement, Ampio now owns 80.9% of Luoxis.

On September 25, 2013, Ampio entered into a Securities Purchase Agreement with a limited number of purchasers, mainly institutional investors, with respect to a registered direct offering of 4,600,319 shares of the Company s common stock, par value $0.0001 per share, at a price of $5.50 per share. Net proceeds from the offering, after deducting offering expenses, were $25 million. No placement agent was used for the offering. The proceeds from the offering will be used 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.

**Known Trends or Future Events; Outlook**

We have not generated any significant revenues and have therefore incurred significant net losses totaling approximately $64 million since our inception in December 2008. The assets we purchased from BioSciences in April 2009 generated minimal revenues prior to their acquisition. We expect to generate operating losses for the foreseeable future, but intend to try to limit the extent of these losses by entering into co-development or collaboration agreements with one or more strategic partners. Although we have raised capital in the past and with net proceeds of $29 million, $15.4 million and $19.4 million through the sale of common stock in 2013, 2012 and 2011, respectively, we cannot assure you that we will be able to secure such additional financing, if needed, or that it will be adequate to execute our business strategy. Even if we obtain additional financing, it may be costly and may require us to agree to covenants or other provisions that will favor new investors over existing shareholders.

Table of Contents

Our primary focus is advancing the clinical development of our core assets: Ampion and Optina. We have previously announced the initiation of a Phase III final pivotal trial of Ampion in osteoarthritis of the knee and a Phase IIb clinical trial of Optina in diabetic macular edema. These trials will be blinded and conducted by third party clinical research organizations. On December 16, 2013, we announced a ten-year lease of a multi-purpose facility containing 19,346 square feet. This facility will include an FDA compliant clean room to manufacture Ampion and will be our new headquarters. The facility is expected to be operational by the summer of 2014.

**Significant Accounting Policies and Estimates**

Our consolidated financial statements have been prepared in accordance with accounting policies generally accepted in the United States of America. The preparation of the consolidated financial statements requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting period. On an on-going basis, management evaluates its estimates and judgments, including those related to recoverability of long-lived assets, fair value of our derivative instruments, allowances and contingencies. Management bases its estimates and judgments on historical experience and on various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. The methods, estimates, and judgments used by us in applying these most critical accounting policies have a significant impact on the results we report in our consolidated financial statements.

***Patents***

Costs of establishing patents consisting of legal fees paid to third parties and related costs are currently expensed as incurred. We will continue this practice unless we can demonstrate that such costs add economic value to our business, in which case we will capitalize such costs as part of intangible assets. The primary consideration in making this determination is whether or not we can demonstrate that such costs have, in fact, increased the economic value of our intellectual property. Legal and related costs which do not meet the above criteria will be expensed as incurred. The $500,000 fair value of the Zertane patents acquired in connection with the March 2011 acquisition of BioSciences is being amortized over the remaining U.S. patent lives of approximately 11 years beginning April 2011.

***In-Process Research and Development***

In-process research and development ( IPRD ) relates to the Zertane product and clinical trial data acquired in connection with the March 2011 business combination of BioSciences. The $7,500,000 recorded was based on an independent third party appraisal of the fair value of the assets acquired. IPRD is considered an indefinite-lived intangible asset and its fair value will be assessed for impairment annually and written down if impaired. Once the Zertane product obtains regulatory approval and commercial production begins, IPRD will be amortized over its estimated useful life. If the commercialization of Zertane becomes impracticable or we abandon this drug, we will expense the $7.5 million IPRD asset.

***Research and Development***

Research and development costs are expensed as incurred. These costs consist primarily of expenses for personnel engaged in the design and development of product candidates; the scientific research necessary to produce commercially viable applications of our proprietary drugs or compounds; early stage clinical testing of product candidates or compounds; expenditures for design and engineering of the ORP product; and development equipment and supplies, facilities costs and other related overhead.

***Stock-Based Compensation***

We account for stock-based payments by recognizing compensation expense based upon the estimated fair value of the awards on the date of grant. We determine the estimated grant fair value of options using the Black-Scholes option pricing model and recognize compensation costs ratably over the vesting period using the straight-line method. Common stock issued in exchange for services is recorded at the fair value of the common stock at the date at which we become obligated to issue the shares. The value of the shares is expensed over the requisite service period.

***Derivatives***

We account for hybrid financial instruments (debentures with embedded derivative features conversion options, down-round protection and a mandatory conversion provision) and related warrants by recording the fair value of each hybrid instrument in its entirety and recording the fair value of the warrant derivative liability. The fair value of the hybrid financial instruments and warrants

Table of Contents

was calculated using a binomial-lattice-based valuation model. We recorded a derivative expense at the inception of each instrument reflecting the difference between the fair value and cash received. Changes in the fair value in subsequent periods were recorded as unrealized gain or loss on fair value of derivative instruments for the hybrid financial instruments and to derivative income or expense for the warrants. The warrants associated with these financial instruments expired on December 31, 2013 and the warrant derivative liability was eliminated.

***Income Taxes***

We use the liability method of accounting for income taxes. Under this method, we recognize deferred assets and liabilities based on the differences between the tax basis of assets and liabilities and their reported amounts in the financial statements that will result in taxable or deductible amounts in future years. We establish a valuation allowance for all deferred tax assets for which there is uncertainty regarding realization.

**Results of Operations Year Ended December 31, 2013, 2012 and 2011 See Notes to Consolidated Financial Statements.**

Results of operations for the years ended December 31, 2013, 2012 and 2011 reflected losses of $24.0 million, $ 11.6 million and $18.4 million, respectively. These losses include non-cash charges related to depreciation and amortization expense, derivative expense, stock-based compensation, stock issued for services and losses on the fair value of debt instruments in the amount of $4.2 million in 2013, $1.5 million in 2012 and $9.2 million in 2011.

***Revenue***

We are a development stage enterprise and have not generated material revenue in our operating history. The $50,000 license revenue recognized in 2013 and 2012 represents the amortization of the upfront payment received from our license agreement. The initial payment of $500,000 from the license agreement with a Korean pharmaceutical company was deferred and being recognized over 10 years.

***Expenses***

***Research and Development***

Research and development costs consist of labor, research and development of patents and intellectual property, stock-based compensation as well as drug development and clinical trials. These costs relate solely to research and development without an allocation of general and administrative expenses and are summarized as follows:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2013 | 2012 | 2011 |
| Labor | $ 1,862,000 | $ 1,424,000 | $ 1,364,000 |
| Patent costs | 1,738,000 | 1,449,000 | 962,000 |
| Stock-based compensation | 1,997,000 | 396,000 | 316,000 |
| Clinical trials and sponsored research | 12,078,000 | 3,756,000 | 1,694,000 |
| Techology license | | | 2,000,000 |
| Consultants and other | 614,000 | 469,000 | 312,000 |
| | $ 18,289,000 | $ 7,494,000 | $ 6,648,000 |

*Comparison of Years Ended December 31, 2013 and 2012*

Research and development expenses increased $10,795,000, or 144%, in 2013 over 2012. This was due primarily to costs associated with the production of study drugs, clinical trials of Ampion and Optina and the Luoxis development of its ORP platform. Labor and stock-based compensation increased due to bonuses paid/accrued and stock options granted in both Ampio and Luoxis as well as the continuing vesting of stock option awards granted in previous years. We continue to maintain and increase our patent portfolio.

*Comparison of Years Ended December 31, 2012 and 2011*

Research and development expenses increased approximately 13% in 2012 over 2011. This was due primarily to costs associated with FDA pre-IND filings for our three major drug candidates, the IND submissions for Ampion and Optina, and clinical trials of Ampion and Optina. We also incurred costs related to the production of the study drugs for the Ampion and Optina trials. We continue to maintain and strengthen our patent portfolio while labor and stock compensation costs were relatively flat.

Table of Contents

***General and Administrative***

General and administrative expenses consist of personnel costs for employees in executive, business development and operational functions; professional fees include legal, auditing and accounting; occupancy, travel and other includes rent, governmental and regulatory compliance, insurance, investor/public relations and professional subscriptions. These costs are summarized as follows:

| | Year Ended December 31, | | |
|---|---|---|---|
| | **2013** | **2012** | **2011** |
| Labor | $ 1,538,000 | $ 1,308,000 | $ 888,000 |
| Stock-based compensation | 1,539,000 | 1,227,000 | 1,671,000 |
| Professional fees | 735,000 | 399,000 | 656,000 |
| Occupancy, travel and other | 1,767,000 | 1,191,000 | 932,000 |
| Directors fees | 206,000 | 252,000 | 357,000 |
| | $ 5,785,000 | $ 4,377,000 | $ 4,504,000 |

*Comparison of Years Ended December 31, 2013 and 2012*

General and administrative costs increased $1,408,000, or 32%, in 2013 over 2012. The increase in labor costs and stock-based compensation primarily relates to the addition of our chief operating officer in December 2012, increased professional staffing in Luoxis, bonuses paid/accrued and stock options granted in both Ampio and Luoxis as well as the continuing vesting of stock option awards granted in previous years. The labor costs in 2012 includes an employment agreement payout to our former CEO. The increase in professional fees is associated with the formation of the subsidiaries for Luoxis and Vyrix and the fees associated with legal defense costs. Occupancy, travel and other increased primarily due to insurance premiums, regulatory and compliance fees and travel expenses.

*Comparison of Years Ended December 31, 2012 and 2011*

There was an overall decrease of approximately 3% in general and administrative costs in 2012 from 2011. Labor costs increased in 2012 as the result of the employment agreement payout to our former CEO upon the granting of an indefinite compassionate leave of absence in January 2012. Stock-based compensation decreased in 2012 due to longer vesting periods being incorporated into new awards, resulting in straight line amortization of the fair value over a longer period. Professional fees consist primarily of legal, audit and accounting costs, public company compliance costs, and consulting related to capital formation. Professional fees decreased in 2012 as compared to 2011 since we had only routine filing and reporting requirements in 2012. In 2011 we had additional professional fees related to the filing of a Form S-4 with the SEC and the acquisition of BioSciences. Travel and investor/public relations costs increased in 2012 as we pursued business development and financing opportunities. Directors fees decreased because only regularly scheduled meetings were held during 2012, compared to 2011 when additional meetings were required. No general and administrative costs are currently being allocated to the research and development activities.

***Derivative Expense***

We recorded approximately ($517,000), $206,000 and ($1.6) million in non-cash derivative income (expense) in 2013, 2012 and 2011, respectively, in connection with our hybrid financial instruments consisting of debentures and related warrants. The expense relates to the fair value at inception and subsequent changes in fair value of the

debentures issued in 2011 and 2010 stemming from the embedded derivative features (conversion options, down-round protection and mandatory conversion provisions) and the changes in fair value of warrants issued in conjunction with the debentures. The debentures were redeemed in 2011 and the December 31, 2013 expiring warrants were all exercised prior to that date.

***Unrealized loss on fair value of debt instruments***

We recorded $5.6 million in non-cash unrealized loss on fair value of debt instruments in the first quarter of 2011. The expense reflects the change in fair value of our debentures prior to their conversion to common stock in February 2011 and stemmed primarily from the increase in our common stock price between December 31, 2010 and February 28, 2011, when the debentures were converted.

***Foreign income tax expense***

The $82,500 of foreign income tax expense in 2011 is the amount of Korean income taxes withheld in connection with the $500,000 payment received for the signing of the license agreement with the Korean pharmaceutical company.

Table of Contents

***Net Cash Used in Operating Activities***

During 2013, our operating activities used approximately $19.1 million in cash. The use of cash was $5.4 million lower than the net loss due primarily to non-cash charges for stock-based compensation, depreciation and amortization, derivative expense and non-cash deferred revenue. Net cash provided in operating activities also included a $522,000 increase in accrued bonuses/salaries and $699,400 increase in accounts payable.

During 2012 our operating activities used approximately $9.7 million in cash. The use of cash was $1.9 million lower than the net loss due to non-cash charges for stock-based compensation, depreciation and amortization and also non-cash deferred revenue and derivative income. Net cash used in operating activities also included a $121,770 increase in prepaid expenses and cash provided by a $570,500 increase in accounts payable.

During 2011 our operating activities used approximately $9.1 million in cash. The use of cash was significantly lower than the $18.4 million net loss, primarily as a result of non-cash charges for depreciation and amortization, stock-based compensation, and derivative and unrealized loss on fair value of debt instruments of $9.2 million. Net cash used in operating activities included the receipt of revenue to be recognized over a ten year period, but was offset by the payment of deferred salaries.

***Net Cash Used in Investing Activities***

During 2013, cash was used to acquire ORP patents on behalf of Luoxis See Note 3 Formation of Subsidiaries. Fixed assets reflect purchases of machinery related to the in process manufacturing facility/clean room, a new server, a lab scope and a Luoxis ORP manufacturing device.

***Net Cash from Financing Activities***

Net cash provided by financing activities in 2013 was $29.4 million which reflects net proceeds from the registered direct placement of $25.0 million, Luoxis private financings of $4.0 million and $0.4 million from the exercise of stock options and warrants.

Net cash provided by financing activities in 2012 was $16 million. During the year, Ampio completed an underwritten public offering, with net proceeds of $15.4 million, options exercised of $618,000 and warrants exercised of $12,322. We also received a repayment of $36,883 related to the stockholders advances from BioSciences made in 2010.

Net cash provided by financing activities in 2011 was $20 million. During the year, Ampio completed private placement and registered direct offerings, with net proceeds of $19.4 million, debentures were issued for $382,000, options exercised of $109,045 and warrants exercised of $155,171. We also received a repayment of $22,660 related to the stockholders advances from BioSciences made in 2010.

**Contractual Obligations and Commitments**

The following table summarizes the commitments and contingencies as of December 31, 2013 which are described below:

| | Total | 2014 | 2015 | 2016 | 2017 | 201 |
|---|---|---|---|---|---|---|