Ampio Pharmaceuticals, Inc.
Form 10-K
February 09, 2012
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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, 2011

¨ **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 incorporation or organization)	**(I.R.S. Employer Identification Number)**
5445 DTC Parkway	**80111**

Suite 925

Greenwood Village, Colorado
(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, 2011 was $177,637,356.

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 9, 2012, 31,113,921 shares of common stock were outstanding.

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This Report on Form 10-K refers to trademarks, such as Optina, Ampion, Zertane and Vasaloc, 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.

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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.

EXPLANATORY NOTE

The Registrant was a smaller reporting company under applicable SEC rules and regulations for the year ended December 31, 2011. The Registrant has determined that it will be an accelerated filer under applicable SEC rules and regulations for the year ending December 31, 2012. In accordance with the transition rules established by the SEC, the Registrant is permitted to use the scaled disclosure requirements applicable to smaller reporting companies in this Annual Report on Form 10-K. The Registrant will be transitioning to the disclosure requirements applicable to accelerated filers beginning with the Registrant s Quarterly Report on Form 10-Q for the quarterly period ending March 31, 2012.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Report on Form 10-K contains forward-looking statements within the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Generally, the use of terms such as will, may, should, continue, believes, expects, intends, anticipates, estimates and sim identify forward-looking statements. All statements other than statements of historical fact contained in this Form 10-K, including statements regarding future events, our future financial performance, business strategy, and our plans and objectives, are forward-looking statements. Without limiting the generality of the preceding sentence, statements contained herein regarding matters that are not historical facts constitute forward-looking statements. Although we do not make forward-looking statements unless we believe we have a reasonable basis for doing so, we cannot guarantee their accuracy.

These forward-looking statements involve known and unknown risks and uncertainties that are difficult to predict, including the risks outlined under Item 1A of Part I, Risk Factors, in this Form 10-K, which may cause our actual results, levels of activity, performance or achievements expressed or implied by these forward-looking statements to differ from expectations. Factors that could cause actual results to differ materially from those contemplated by the forward-looking statements include, among others, the following:

- the results and timing of our clinical trials, particularly the Optina and Ampion trials;
- the regulatory review process and any regulatory approvals that are issued or denied by the FDA, the EMEA, or other regulatory agencies;
- our need to secure collaborators to license, manufacture, market and sell any products for which we receive regulatory approval in the future;
- the results of our internal research and development efforts;
- the commercial success and market acceptance of any of our product candidates that are approved for marketing in the United States or other countries;
- the safety and efficacy of medicines or treatments introduced by competitors that are targeted to indications which our product candidates have been developed to treat;
- acceptance and approval of regulatory filings;

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

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

our plans to develop other product candidates.

You should not place undue reliance on our forward-looking statements in this Form 10-K because the matters they describe are subject to known and unknown risks, uncertainties and other unpredictable factors, many of which are beyond our control. Our forward-looking statements are based on the information currently available to us and speak only as of the date of this Form 10-K. New risks and uncertainties arise from time to time, and it is impossible for us to predict these matters or their effect on us or the extent to which any factor, or combination of factors, may cause our actual results to differ materially from those contained in any forward-looking statements. Over time, our actual results, performance or achievements will likely differ from the anticipated results, performance or achievements that are expressed or implied by our forward-looking statements, and such differences might be significant and materially adverse to our investors. We have no duty to, and do not intend to, update or revise the forward-looking statements in this Form 10-K after the date of this Form 10-K except to the extent required by the federal securities laws. You should consider all risks and uncertainties disclosed in our filings with the SEC, all of which are accessible on the SEC s website at www.sec.gov.

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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.

Estimates of historical growth rates in diabetes and other diseases are not necessarily indicative of future growth rates. When referring to clinical indications, observations, and treatment modalities, we relied on clinical data evaluated by, and publications authored or co-authored by, Dr. Bar-Or, our chief scientific officer, and published information from medical journals and other sources concerning clinical trials conducted by others and regulatory approvals obtained for other pharmaceutical products. With respect to diabetes-related conditions, we relied in part also on the Proceedings of the American Academy of Ophthalmology Preferred Practice Patterns: Diabetic Retinopathy, 2008 and *Clinical Effect of Danazol in Patients with IgA Nephropathy,* Tomino, *et al*, Japan J. Med.; 26(2): 162-166. In estimating the market size for Ampion, we referred in part to information published by Datamonitor, *Stakeholder Insight: Osteoarthritis,* DMHC1907, December 2003.

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AMPIO PHARMACEUTICALS, INC.

PART I

Item 1. ***Business***

Overview and General Discussion of the Business

We are a development stage biopharmaceutical company engaged in discovering and developing innovative, proprietary pharmaceutical drugs and diagnostic products to identify, treat, and prevent a broad range of human diseases including metabolic disorders, eye disease, kidney disease, acute and chronic inflammation, and male sexual dysfunction. 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 acquisition. 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.

Acquisition of BioSciences

In April 2010, we announced the execution of a letter of intent to acquire BioSciences. We and BioSciences executed a definitive merger agreement on September 4, 2010 which was adopted and approved by consent of a majority of the Ampio shareholders on November 9, 2010. The final consent agreement was approved by both parties January 5, 2011 and the merger closed on March 23, 2011. BioSciences owned the rights to one product, Zertane™, and held 32 issued patents and 31 pending patent applications related to the product. Zertane™ is a new use for tramadol hydrochloride, and was approved for marketing as a non-controlled analgesic in 1995. As of December 31, 2011, there are 32 issued patents and 34 pending applications, 3 of which are allowed related to the product. The purpose of the BioSciences acquisition was to unify our management team and ownership as (i) BioSciences owned and donated back to Ampio, 3,500,000 shares of Ampio common stock, or approximately 20% of the outstanding Ampio shares of common stock, (ii) Ampio s Zertane™ Product Manager, Bruce G. Miller, was also the president, a director and a principal Class B shareholder of BioSciences, (iii) Ampio s chief scientific officer and director, Dr. David Bar-Or, was a former executive officer and director, and a principal Class B shareholder of BioSciences, (iv) Richard B. Giles, a shareholder of BioSciences, is a member of the Board of Directors and shareholder of Ampio, and (v) several other Ampio investors were also shareholders of BioSciences.

The aggregate consideration paid by Ampio to BioSciences shareholders in the merger was 8,473,789 shares of Ampio common stock which is net of shares exchanged for options in settlement of a dispute with three option holders of BioSciences. This consideration includes the shares payable to holders of in-the-money BioSciences stock options and warrants, and holders of two BioSciences promissory notes, outstanding immediately prior to the effective time of the merger. 435,717 out-of-the-money options to purchase Ampio shares at an average price of $1.54 were also issued as consideration.

Acquisition of Product Technology License

In December 2011, Ampio acquired all rights, title and interest in and to the manufacturing rights and know-how relating to an oral disintegrating tablet (ODT) for Zertane™ for $2,000,000 plus potential future consideration based on net sales of the product. We believe that this purchase will aid in the regulatory approval and commercialization of Zertane™.

Business Model

We are focused on developing proprietary drugs and diagnostic products which capitalize on our own internal discoveries and our intellectual property. This intellectual property includes owned and assigned patents, filed patent applications, exclusive licenses, and trade secrets and

know-how, some of which may be the subject of future patent applications. Our intellectual property is strategically focused on three primary areas: new indications for previously approved drugs, New Molecular Entities (NMEs), and rapid point-of-care tests for diagnosis, monitoring and screening. Promising discoveries are evaluated, with a particular emphasis on candidates for which we believe there is a relatively quick path to commercialization. This path could be through identifying new applications, indications, dosing, or chemical combinations for compounds previously approved as safe and effective by the Federal

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Drug Administration (FDA) or other established governmental regulatory agencies. Known as drug repositioning, we believe this strategy reduces the risk of product failure due to adverse toxicology, leads to more modest investments during development, and may achieve more rapid marketing approval. With our focus on discovery and development, we will likely seek partners to help us ultimately commercialize our discoveries in the United States, Europe, and additional international markets.

We are currently in the clinical stage of development on three product candidates that were discovered by Dr. Bar-Or and chosen from our pre-clinical pipeline based upon ultimate market potential and our belief that these candidates had a relatively shorter pathway to commercialization. Two of these product candidates, Zertane™, in development for premature ejaculation (PE) and Optina™, in development for diabetic macular edema (DME), are repositioned drugs for which we have secured or are securing U.S. and international patent protection covering their unique formulation, application, or newly discovered formulas. Our third clinical stage product, Ampion™, is in development for treatment of osteoarthritis of the knee and is covered by a pharmaceutical composition of matter patent. However, Ampion™ is derived from human serum albumin, an already approved human blood product. As such, we believe Ampion™ will be regulated by the Center for Biologics Evaluation and Research (CBER) division of the FDA. Biologics are controlled by separate legislation from drugs and may have relatively fewer safety concerns in some instances as they are derived from the human body. Given the depth of our pre-clinical pipeline, we may choose to collaborate, license, or sell discoveries that we choose not to develop internally.

New Molecular Entities

While our products furthest along in clinical development are primarily repositioned drugs, we have several new molecular entities in our pre-clinical pipeline. As announced in our press release on November 16, 2011, we have received PTO notification of the allowance of two U.S. patents on new chemical entities that have been developed internally. The first patent is directed to a unique class of compounds that combine elements of diketopiperazines (same class as Ampion) and methylphenidate derivatives. The second patent is directed to novel derivatives of methylphenidate (Ritalin). Both patents contain not only use claims for these novel compounds, and pharmaceutical compositions containing them, but also composition of matter claims. We believe that these compounds could have specific application to brain tumors as well as other malignancies. We could either continue to develop these products internally, or seek another pharmaceutical company partner to do so.

Our Product Pipeline

The following table summarizes the status of our products in clinical development.

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Ampion™: Biologic to Treat Inflammatory Conditions and Autoimmune Diseases

Ampion™ is a non-steroidal biologic, aspartyl-alanyl diketopiperazine, referred to as DA-DKP. This compound is derived from two amino acids from human albumin, and is designed to treat chronic inflammatory and autoimmune diseases. Because it is a naturally occurring human molecule, DA-DKP is present in the body and can be detected in plasma. Early in the discovery of DA-DKP by us, it became apparent that it is the natural by-product of commercially available human serum albumin (HSA). In the manufacture of HSA, an FDA approved human biologic, DA-DKP is the result of cleavage and cyclization from the end (N-terminus aspartate and alanine) of albumin just as we believe occurs inside the human body. Many referenced publications now mention the pharmacological, including anti-inflammatory, properties, of HSA. HSA has been used topically in the eye to decrease irritation and is now the subject of a large clinical trial, ClinicalTrials.gov Identifier NCT00796419, to decrease inflammation in the lung after trauma. It is our belief that one of the active anti-inflammatory ingredients in HSA is the DA-DKP compound.

Ampion™ was shown in vitro to have significant effects on inflammation and other physiological and metabolic parameters. Dr. Bar-Or has published a number of studies and articles on the anti-inflammatory immune response of DA-DKP. There are numerous clinical areas in need of improved anti-inflammatory medications. The figure below shows a group of disease states that we believe Ampion™ could be used to treat.

Early in vitro and animal studies conducted by us and our predecessors using Ampion™ showed indications of efficacy in treating autoimmune diseases such as Multiple Sclerosis (MS). However, we believe that clinical trials in Multiple Sclerosis would require substantial financial and time commitments not considered viable at this time. Other clinical indications, such as Osteoarthritis, have the advantage of high prevalence within the population and well defined outcomes. Therefore, we have decided to pursue these indications as a first step to ascertain the safety and efficacy of the Ampion™ compound. Assuming a successful outcome of these initial clinical trials and proof of concept studies, we intend to actively pursue other indications such as inflammatory conditions of the eye, perioperative inflammation, and autoimmune diseases such as Crohn s disease, rheumatoid arthritis, Sjogren s syndrome, and Multiple Sclerosis. We will evaluate the potential and may choose to develop Ampion™ for these additional indications with or without collaboration with a partner.

We control a patent for pharmaceutical compositions that include DA-DKP and a patent for a method for the production of DA-DKP as a synthetic (small molecule component).

If we were to produce the molecule synthetically, we believe that most regulatory authorities would consider it an NME and, as such, would require detailed animal toxicology studies as well as extensive Phase I, II and III human studies to demonstrate safety. We believe that these studies would take 5 to 7 years and cost several hundred million dollars to complete. Alternatively, the presence of Ampion™ in the already FDA approved HSA, presents a unique option to expedite this process. As such, we have moved forward with a filtrate of HSA as an injectable for our osteoarthritis trials and commenced human efficacy studies in 2011.

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In October 2011, we released a preliminary analysis of a 60 patient Ampion™ trial for patients with osteoarthritis of the knee in Australia. Sixty patients were injected with a steroid (standard of care) with or without Ampion™. Initial results showed Ampion™ well tolerated with no additional difference in adverse events and further demonstrated synergistic efficacy in combination with the steroid. These results permitted expansion of the trial to 42 patients with an addition of two arms comparing Ampion™ as a mono-therapy versus vehicle (normal saline) which we believe will demonstrate its efficacy as an anti-inflammatory. Preliminary analysis of the pain scores portion of the trial demonstrated positive results, suggesting that Ampion may be a therapeutic alternative to steroids for osteoarthritis with a very favorable safety profile. One simple way to analyze the data is to determine the overall change in pain scores at different time points after the knee injections with Ampion or vehicle control. Pain trials are notorious for involving a significant placebo effect which usually tends to fade with passage of time. The overall difference in pain score was 41% for Ampion at 30 days post injection compared to baseline. The placebo vehicle control (saline) showed a difference of 28% over the same time period and was not statistically significant. With Ampion , 64% of patients had a clinically meaningful improvement (2 or more on the 1-10 pain scale) and 18% did not benefit. With the vehicle control/placebo, no clear difference was seen as 40% showed improvement and 40% did not benefit (Chi square=0.125).

This human data, along with our extensive in-vitro data elucidating the mechanisms of action for Ampion™, will be the basis of discussions with the FDA for definitive clinical trials. We have filed our pre IND meeting request with the FDA and we hope to rapidly gain clarity and initiate the definitive trial(s) in the second half of 2012.

Osteoarthritis (OA) is a degeneration of the joints, including articular cartilage, subchondrial bone, and periarticular muscles. The disease is progressive and symptoms include joint pain and inflammation, stiffness, crepitus, and limitation of movement. OA is one of the major causes of pain in the world and there are estimated to be over 80 million sufferers worldwide. In the US, there are over 29 million OA patients, of which roughly 10 million have OA of the knee. There are a variety of pharmacological treatments for the symptoms of OA, including oral NSAIDs and COX-2 inhibitors, as well as topical NSAIDs, injectable steroids and injectable hyaluronic acids. We believe that Ampion™ will compete directly with the injectables, but depending upon the ultimate safety and efficacy of the product, it might also replace some of the other forms of treatment. There are over 3 million OA patients in the US that receive some form of injection as a treatment per year. One of the market leader hyaluronic acids, Genzyme s Synvisc, reported over $300,000,000 in revenues in 2011, and clinical studies have shown modest efficacy relative to control. Steroid injections are generic, effectively off-label, and concerns have been expressed that chronic steroid injections could lead to joint destruction and tissue atrophy.

Optina™: Repositioned Drug to Treat Diabetic Macular Edema (DME)

Optina™ is an orally-administered compound in development for the treatment of diabetic macular edema (DME). Optina™, a low-dose danazol, is based on a derivative of the synthetic steroid ethisterone. Danazol was approved by the FDA in the 1970 s for endometriosis and, more recently, for other chronic indications such as hereditary angioedema. Dr. Bar-Or discovered an unexpected activity: low doses of danazol reverse inflammation induced increases in the permeability of blood vessels, thus reducing vascular leakage. This effect may reduce the vasogenic edema produced from multiple diseases, including diabetes. The effect of danazol is systemic , meaning that it works throughout the whole body not just in isolated regions. This oral therapy works inside the vessel and may be beneficial to multiple organs simultaneously (e.g. both the eyes and kidneys of diabetic patients).

The specific dosage is proprietary and subject to present patent filings. However, the dose is below any approved dosage tablet on the market. The existing indications of Danazol all appear to require a dosage that Dr. Bar-Or has established has no beneficial vascular effect and may, in fact, worsen vascular permeability. We believe that published literature already shows that doses lower than what is currently approved are ineffective in treatment of these existing indications. Therefore, we believe that generic approval of Danazol based on existing indications will not be possible at doses effective for treating DME. This unexpected finding that use of Danazol at low doses inhibits vascular hyperpermeability will support patentability of current patent claims. Further, since existing approved uses of Danazol are at higher doses than what can be effectively used to treat vascular hyperpermeability, we believe that completion for treatment of DME from off-label use of Danazol for existing approved uses will not be significant.

We previously entered into a contract with St. Michael s Hospital in Toronto, Canada, to conduct a clinical trial of Optina™. Patient enrollment for this trial began in January 2011. The human clinical trial is titled, A Randomized, Double-masked, Placebo-Controlled, Parallel Treatment Group, Dose-Ranging, Efficacy and Safety Study of Oral (Optina™) Capsules in Subjects with Diabetic Macular Edema. This ongoing trial is still in the patient recruitment stage. Patients either receive a placebo or Optina™ with the primary end point being a direct physical measurement of the edema at the back of the eye, measured with optical coherence tomography. The secondary endpoint of visual acuity is measured with lines on an eye chart. We anticipate the results of this trial will be available in mid-2012 and will provide the basis for discussion of pivotal trials to be conducted in the United States. The greater purpose of the secondary endpoint is to accurately calculate the size of study required to demonstrate efficacy using visual acuity, the current FDA guidance. Our current hypothesis is that our trials will be shorter than those for alternative treatments for this indication based on our assertion that this daily oral therapy is only effective during administration. Early indications also suggest that low dose danazol may also be efficacious in decreasing vascular permeability in the kidneys of diabetic patients

and, therefore, potentially delaying the onset of diabetic nephropathy. Development of Vasaloc™, another of our product candidates, as a separate indication is pending supportive data from the Optina trial and discussion with regulators.

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In 2011, we supported an FDA exempted, investigator directed trial using commercially available danazol recompounded into a low dose danazol spray for the reduction of symptoms of allergic rhinitis. We believe that this study, though small (N=20), demonstrated the ability of danazol to reduce the edema (stuffiness) in the nasal mucosa. This study added to the experience of safety and efficacy in the treatment of edema in another tissue of the human body.

We believe Optina will be eligible for regulatory approval in the U.S. as a §505(b)(2) New Drug Application submission and in the EU under its hybrid abridged procedure. We plan to go to the FDA to discuss the regulatory pathway and structure of the clinical trials needed for approval in the second half of 2012.

The market size for DME is difficult to measure but the demographics suggest a large potential market exists. The American Diabetes Association reports that 20.8 million people in the U.S. have diabetes and another 54 million are pre-diabetic with 20% of type-2 diabetic patients having retinopathy when diagnosed. According to the World Health Organization, approximately 5 million individuals have diabetic retinopathy, accounting for 5 percent of world blindness. Over 360 million people worldwide are projected to have diabetes and its complications by 2030 with almost all patients with type-1 diabetes and more than 60% of patients with type-2 diabetes developing retinopathy. The International Diabetes Federation estimates that 285 million people around the world have diabetes and approximately 14% of people with diabetes have DME. According to the American Academy of Ophthalmology, the prevalence of DME increases to 29% for people with diabetes who use insulin for more than 20 years. By 2030, the incidence of diabetes is expected to rise to 438 million people worldwide, and the incidence of diabetes-related conditions like DME, diabetic retinopathy, and diabetic nephropathy are expected to continue to increase proportionately

If untreated, DME leads to moderate vision loss for one out of four people with diabetes over a period of three years and can lead to blindness over a period of seven years. Existing therapies for diabetic retinopathy, DME and the wet form of Age Related Macula Degeneration (AMD) include focal and grid laser therapy, which is the current standard of care, as well as photodynamic therapy, surgery, and intravitreal treatment, or IVT, using Lucentis, Avastin, or Macugen. Lucentis is costly compared to alternative injection therapies, while Avastin is currently approved only for cancer treatment and is being used off-label by ophthalmologists to treat DME and wet AMD. Macugen recently completed a Phase III trial in which subjects were given injections in the eye as often as every six weeks in both the first and second year of the trial, which resulted in patients gaining 5.2 letters of vision compared to 1.2 letters for patients receiving a sham injection. There are currently no oral medications available for treatment of DME and wet AMD. We believe Optina™ has the potential to effectively treat DME and wet AMD without costly laser therapy and without requiring ongoing injections of pharmaceuticals in the eye. For these reasons, we believe Optina™ represents a significant Phase II stage clinical opportunity.

Having developed over four decades of experience in human use worldwide, we believe Optina™ has demonstrated an acceptable safety profile that supports treatment of diabetic eye disease. We anticipate that Optina™ can be offered to patients in a variety of formulations, including oral tablets, extended release implants, local injections and topically as eye drops. These formulations can increase bioavailability to the eye, may increase patient compliance and could provide additional barriers to competition.

We have filed method of use and composition patent applications for Optina™ in a variety of ocular and other indications in the U.S. and internationally. The patent portfolio strategy is to pursue protection for both the market areas we are pursuing and the clinical data being generated.

Zertane ™

Zertane ™ is a new use for tramadol hydrochloride, which was approved by the FDA for marketing as a non-controlled analgesic in 1995. Based on the results of our Phase III clinical trial, which were announced in June 2011, we believe Zertane ™ can be an effective oral medication to treat premature ejaculation (PE) in men. PE is the most common form of male sexual dysfunction and has a major impact on the quality of life for many men and their partners. The market opportunity may be large and, depending on the definition used (less than one minute or less than two minutes), the incidence is estimated to be 3 to 23% of males suffering from PE. According to Australia s Keogh Institute of Medical Research, PE is the most common sexual complaint in males. At present, no drug has been approved by the FDA for the treatment of PE. Only one product has been formally approved anywhere in the world for PE; Johnson & Johnson s Priligy, an orally administered anti-depressant in the SSRI class, which has been approved in 25 countries outside of the US and is actively promoted in 14 of these countries.

We believe that our unique formulation has numerous advantages over uncontrolled use of the generic tramadol. First, we have obtained the rights to a patented orally disintegrating tablet (ODT) formulation which is under license from the manufacturer. The ODT formulation is convenient and has the potential to speed absorption. In addition, based on the extensive clinical trials conducted to date, we have identified the concentration we believe has maximum beneficial effect and the least side effects: 62 mg. Decreasing the dosage to 50 mg creates a small but significant increase in therapeutic failure. Increasing the dosage to 100 mg has no

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significant effect on preventing PE but significantly increases side effects such as erectile dysfunction. We also believe that the proposed packaging of an F1 rated triple tablet blister pack significantly limits the risk of abuse and misuse as compared to the tramadol 30 tablet bottle. We believe that regulatory approval of Zertane™ would greatly alleviate concerns of physicians or pharmacists who would like to provide tramadol for this condition. Not only does it create a regulated drug supply with accurate dosage, impurity and stability testing in an ODT format, it provides indication specific product insert sheets for patient information of how best to use it to get the greatest effect with the least risk.

Our Phase III clinical trial for Zertane™ was a randomized, double-blind, placebo-controlled, multi-center study to evaluate the efficacy and safety of two doses of Zertane™ for the treatment of PE. The study was conducted at 62 sites in 11 countries in Eastern and Western Europe and included 604 intent-to-treat patients. The clinical study demonstrated statistically significant efficacy and safety for Zertane in treating PE, utilizing co-primary endpoints of Intravaginal Ejaculatory Latency Time (IELT) and a Premature Ejaculation Profile (PEP). We are in the process of preparing our regulatory dossier for Zertane and expect to submit the dossier to the Australian regulatory authority, the TGA, in 2012. Assuming that we receive regulatory approval promptly thereafter, we would expect to begin generating revenues for Zertane beginning in mid to late 2013. In the second quarter of 2012 we also expect to request a pre IND meeting with the FDA.

We are actively seeking partners to help commercialize Zertane™ in the US and worldwide. For example, in September 2011, we entered into a license, development and commercialization agreement with Daewoong Pharmaceuticals Co., Ltd., in South Korea, which grants the pharmaceutical company exclusive rights to market Zertane™ in South Korea for the treatment of PE and for a combination drug to be developed, utilizing Zertane™ and an erectile dysfunction drug. We are in discussions with other parties about other potential licensing and distribution opportunities

Pre-Clinical Pipeline

It has been widely reported that the average cost of developing a NME from discovery to launch is more the $800 million. However, this cost reflects failed research efforts, the estimated value of alternative investments, and is based also on the experience of a sample of large pharmaceutical firms. Our development strategy for NMEs is to obtain laboratory and animal study evidence that a drug is safe and effective enough for human test through rapid, low-cost preclinical proof-of-concept (POC) studies. Preclinical POC studies involve collecting pharmacokinetic, toxicology and safety data in a cost-effective and timely manner.

We believe that drugs derived from naturally-occurring peptides or that are analogues of previously approved drugs may have a higher chance of success in development. We have two classes of NMEs that have shown biological activity in the laboratory, including drug candidates that have been successfully tested for efficacy in animal models.

The first class of NMEs we are testing are nine compounds which are derivatives of methylphenidate, a drug approved for treatment of attention-deficit hyperactivity disorder, Postural Orthostatic Tachycardia Syndrome, and narcolepsy, most commonly known under the trade name Ritalin. Dr. Bar-Or has synthesized and applied for patents for these nine compounds which have demonstrated anti-angiogenesis and anti-metastasis properties. The methylphenidate derivatives are being considered for the treatment of Glioblastoma multiforme (a fatal brain cancer), inflammatory breast cancer and for autoimmune/inflammatory conditions, including ophthalmic disorders. We have also conducted early research into how copper chelating peptides, which would also be NME compounds, can be used to treat Acute Coronary Syndrome, or ACS, and strokes. Because of the nature and extent of clinical trials needed to obtain regulatory approval for NMEs, we will likely out-license these compounds to collaborators at an early stage in development.

In Vitro Diagnostics

Diagnostics serve a key role in the health value chain by influencing the quality of patient care, health outcomes and downstream resource requirements. From consumer-friendly at-home pregnancy and glucose monitoring tests to more complex automated laboratory-based systems, these tests are often first-line health decision tools. While diagnostics comprise less than 5% of hospital costs and about 1.6% of all Medicare costs, their findings are commonly believed to influence as much as 60-70% of health care decision-making. The value of diagnostics accrues not only to clinicians and patients, but to health care managers, third-party payers and quality assurance organizations that use diagnostic performance to measure and improve health care quality.

Oxidation-reduction potential is a tightly controlled bodily parameter, much like the vital signs routinely measured in medical practice temperature, heart rate, respiratory rate, blood pressure and oxygen saturation of blood. Abnormal changes in oxidation-reduction potential are closely associated with poor outcomes in critically ill patients, including heart attack and pneumonia. Rapid results are essential for optimal treatment adjustments in critical care areas such as emergency and intensive care departments. Oxidation-reduction potential results may also help determine which patients are at high risk of early readmission at hospital discharge, especially patients with heart attack, heart failure,

stroke, and pneumonia.

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Numerous scientific studies confirm the clinical value of measuring oxidative stress. Recently, a large assortment of blood and cell tests have been used in research studies to measure separate biomarkers of oxidative stress, such as lipid peroxidation, protein oxidation and total antioxidants, but currently several of these separate biomarker test results are needed to start to assess total oxidative stress. We believe no practical or efficient method currently exists for measuring these oxidative stress biomarkers in a clinical setting. Oxidative stress is often a marker for inflammation, which in turn indicates the presence of disease-related processes or developing conditions.

We are developing a handheld Oxidation-Reduction Potential (ORP) diagnostic device for use at home or in healthcare facilities that will measure the oxidants/antioxidant balances in human blood and plasma. The ORP device is intended to provide the first integrated measure of total oxidative stress status for clinical practice. This device is being developed as a battery-powered unit using a drop of whole blood (or plasma) exposed to disposable electrode strips to provide a rapid test result that will measure the redox balance in human blood.

The ORP device is currently being prototyped and the first prototypes are now being prepared for testing. We are developing a disposable electrode for use in the ORP device and have calibrated the device to measure oxidation reduction potential while taking into account various factors that may affect oxidative stress.

The pivotal clinical trials will use already available full patient samples of blood plasma to confirm efficacy with certain clinical indications and provide data for a 510(k) submission to the FDA. To obtain 510(k) clearance, we must submit a premarket notification demonstrating that the proposed device is substantially equivalent to a device legally marketed in the U.S. for which a premarket approval application (PMA) was not required. We believe that there is a predicate device for ORP that was used to test the viability of organs for transplant. The FDA s goal is to review and act on each 510(k) within 90 days of submission, but it may take longer based on requests for additional information by the FDA. Most 510(k)s do not require supporting data from clinical trials, but the FDA may request such data. We have several other research initiatives underway at this time. However, these initiatives are early-stage and are not yet capable of being assessed for commercialization.

Business Strategy

Our disciplined innovation process is built on clinical observations and patient data gathered under appropriate IRB supervision from clinicians who collaborate with Dr. Bar-Or. Dr. Bar-Or is in charge of the research departments at two of the three Level I trauma centers in the State of Colorado, at which over 120,000 emergency room consultations take place annually. Dr. Bar-Or s clinical team includes biochemists, epidemiologists, molecular biologists, computational biologists and nursing staff. In collaboration with other professional colleagues who provide advisory input, such as vascular surgeons, orthopedic surgeons, neurologists, nephrologists and ER specialists, Dr. Bar-Or uses a multidisciplinary approach to evaluate clinical interactions that direct further research.

Once product candidates are identified and clinical efficacy for one or more indications is initially determined, we focus our development work on advancing product candidates that we believe offer significant therapeutic advantages over currently available treatments and which represent large potential markets. We look to advance product candidates that also address multiple clinical indications, have proven safety profiles, and which can timely demonstrate clinical efficacy. We intend to continue to maintain a diversified product candidate pipeline to mitigate risks associated with pharmaceutical development and increase the likelihood of commercial success.

During the discovery process, we review pertinent scientific literature and conduct searches of patent records in order to make a preliminary determination of patentability. As some of our product candidates are repositioned drugs, the nature and extent of potentially available patent protection is central to our development decisions. Although we are in early clinical testing of two NMEs, we also target discovery and development of new uses for approved drugs because these drugs are based on compounds or medicines already approved by the FDA and/or the EMEA. We believe these drug product candidates may receive faster regulatory approvals than NMEs, thus extending the period during which these product candidates will enjoy patent protection for commercialization.

In order to expedite regulatory approval and commercialization of our currently identified primary drug candidates, we are seeking clarity with the FDA and have filed or are preparing to file pre IND meeting requests. We plan also to outsource manufacturing, and, when deemed appropriate, to out-license to collaborators the rights to sell and market product candidates that receive regulatory approval within or outside the U.S. We may also opportunistically enter into agreements with collaborators prior to licensing that may be country, region or application specific and that may lead to sublicenses. Although such outsourcing may reduce income derived from any sales of approved products, our business model is premised on carefully controlling fixed overhead and development costs, creating a catalyst to value by identifying patent-protectable product candidates with significant commercial potential and clinical efficacy, and to advance those product candidates through clinical trials and the regulatory approval process in order to position an approved product for global market introduction by a licensee.

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We believe there are a number of potential licensees for any products that receive regulatory approval, including pharmaceutical and biotechnology companies with substantial manufacturing facilities, established sales organizations, and significant marketing resources. If a product candidate receives regulatory approval and may have the potential to be successfully commercialized, we would evaluate our business model based on the current business and regulatory environments, with the possibility of shifting our business model and substantially increase our retained development activities, engage in manufacturing, or develop a sales and marketing organization. We intend to maximize shareholder value by strategically identifying, developing and advancing patent-protectable product candidates to the point that a compelling rationale exists for a collaborator to license any product receiving regulatory approval. If any of our product candidates are licensed to a collaborator, we may marginally increase our operating budget to conduct additional research, but we will intentionally continue to outsource clinical trials, manufacturing, and marketing to collaborators in order to meet our business objectives.

Regulation

The preclinical and clinical development, testing, manufacture, safety, efficacy, labeling, storage, distribution, promotion, sale and export, reporting, and record-keeping of our product candidates are subject to extensive regulation. The FDA and corresponding state agencies are primarily responsible for such regulation in the United States, and similar regulatory agencies in foreign countries are responsible for regulation of our product candidates outside the United States. We must provide the FDA and foreign regulatory authorities, if applicable, with clinical data that appropriately demonstrate each product candidate s safety and efficacy in humans before the product candidate can be approved for the targeted indications. We are unable to predict whether regulatory approval will be obtained for any product candidate we are developing or plan to develop. The regulatory review and approval process can take many years, is dependent upon the type, complexity, and novelty of the product, requires the expenditure of substantial resources, involves post-marketing surveillance, and may involve ongoing reporting or monitoring.

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. Even 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; and
- 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 the 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.

The ability to market a product outside of the United States is contingent upon receiving a marketing authorization from appropriate regulatory authorities. Foreign regulatory approval processes typically involve risks similar to those associated with obtaining FDA approval and may include additional risks. In addition, 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. We cannot assure you any of our product candidates will prove to be safe or effective, will receive regulatory approvals, or will be successfully commercialized.

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 or on our behalf are subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse events or experiences. Drug manufacturers and their subcontractors are required also 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 current Good Manufacturing Processes, or cGMP. The cGMP impose rigorous procedural and documentation requirements upon us and any manufacturers engaged by us. 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 our contract manufacturers must provide certain updated safety and efficacy information to the FDA and other regulatory agencies. 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 product also must be in compliance with FDA and Federal Trade Commission, or 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.

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The FDA s policies may change and additional government regulations may be enacted which could prevent or delay regulatory approval of our product candidates. Moreover, increased attention to the containment of health care costs in the United States and in foreign markets could result in new government regulations that could cause an increase in our compliance, manufacturing, or other operating expenses, or decrease our gross margins on any product candidates we commercialize.

Regulatory Approval Process for NMEs

FDA regulations require us to undertake a long and rigorous process before any of our NME product candidates may be marketed or sold in the United States. This regulatory process typically includes the following steps:

- the performance of satisfactory preclinical laboratory and animal studies under the FDA s Good Laboratory Practices regulation;
- the development and demonstration of manufacturing processes which conform to FDA-mandated cGMP;
- the submission and acceptance of an Investigational New Drug (IND) application which must become effective before human clinical trials may begin in the United States;
- 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;
- the successful completion of a series of adequate and well-controlled human clinical trials to establish the safety, purity, potency and efficacy of any product candidate for its intended use; and
- the submission to, and review and approval by the FDA of a New Drug Application (NDA) before any commercial sale or shipment of a product.

This process requires a substantial amount of time and financial resources which we currently do not possess. Even if we obtain financing that can be directed to the NME product candidate approval process, there is no assurance this process will result in the granting of an approval for any of our product candidates on a timely basis, if at all.

Preclinical Testing

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, analytical data and the clinical trial protocol, 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 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. 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 requirements.

Clinical Trials

Human clinical trials are typically conducted in three sequential phases:

Phase 1.	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.
Phase 2.	During this phase, 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.	If and when one or more Phase 2 trials demonstrate that a specific dose or range of doses of a product candidate is likely to be effective and has an acceptable safety profile, one or more 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. The successful demonstration of clinical efficacy and safety in one or more Phase 3 trials is typically a prerequisite to the filing of a NDA for a product candidate.

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We cannot be certain that we will successfully complete the Phase 1, Phase 2, or Phase 3 testing of our product candidates within any specific time period, if at all. Furthermore, The FDA or an IRB may suspend or terminate a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

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 our contract manufacturers 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.

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