BIODELIVERY SCIENCES INTERNATIONAL INC
Form 10-K
March 16, 2015
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

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

For the fiscal year ended December 31, 2014

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

For the transition period from _____ to _____

Commission file number 001-31361

BioDelivery Sciences International, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**35-2089858**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
4131 ParkLake Avenue, Suite #225	
Raleigh, NC	**27612**
(Address of principal executive offices)	**(Zip Code)**

Issuer s telephone number: 919-582-9050

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Name of exchange on which registered**
Common stock, par value $.001	**Nasdaq Capital Market**

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 Act. Yes ¨ No x

Indicate by 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 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, or 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 the voting and non-voting common equity held by non-affiliates as of June 30, 2014 was approximately $310,944,998 based on the closing sale price of the company s common stock on such date of $12.07 per share, as reported by the NASDAQ Capital Market.

As of March 12, 2015, there were 52,320,866 shares of company common stock issued and 52,305,375 shares of company common stock outstanding.

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BioDelivery Sciences International, Inc.

Annual Report on Form 10-K

For the fiscal year ended December 31, 2014

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Unless we have indicated otherwise, or the context otherwise requires, references in this Report to BDSI, the Company, we, us and our or similar terms refer to BioDelivery Sciences International, Inc., a Delaware corporation and its consolidated subsidiaries.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Report and the documents we have filed with the Securities and Exchange Commission (which we refer to herein as the SEC) that are incorporated by reference herein contain forward-looking statements, within the meaning of Section 27A of the Securities Act of 1933, as amended (or the Securities Act) and Section 21E of the Securities Exchange Act of 1934, as amended (or the Exchange Act), that involve significant risks and uncertainties. Any statements contained, or incorporated by reference, in this Report that are not statements of historical fact may be forward-looking statements. When we use the words anticipate, believe, could, estimate, expect, intend, ma predict, project, will and other similar terms and phrases, including references to assumptions, we are identifying forward-looking statements. Forward-looking statements involve risks and uncertainties which may cause our actual results, performance or achievements to be materially different from those expressed or implied by forward-looking statements.

A variety of factors, some of which are outside our control, may cause our operating results to fluctuate significantly. They include:

our plans and expectations regarding the timing and outcome of research, development, commercialization, manufacturing, marketing and distribution efforts relating to our BEMA® (as defined below) drug delivery technology platform and any of our approved products or product candidates;

the domestic and international regulatory process and related laws, rules and regulations governing our technologies and our approved and proposed products and formulations, including: (i) the timing, status and results of our or our commercial partners filings with the U.S. Food and Drug Administration and its foreign equivalents, (ii) the timing, status and results of non-clinical work and clinical studies, including regulatory review thereof and (ii) the heavily regulated industry in which we operate our business generally;

our ability to enter into strategic partnerships for the development, commercialization, manufacturing and distribution of our products and product candidates;

our ability, or the ability of our commercial partners, to actually develop, commercialize, manufacture or distribute our products and product candidates, including for BUNAVAIL®, which is the first product we are self-commercializing;

our ability to generate commercially viable products and the market acceptance of our BEMA® technology platform and our proposed products and product candidates;

our ability to finance our operations on acceptable terms, either through the raising of capital, the incurrence of convertible or other indebtedness or through strategic financing or commercialization partnerships;

our expectations about the potential market sizes and market participation potential for our approved or proposed products;

the protection and control afforded by our patents or other intellectual property, and any interest patents or other intellectual property that we license, of our or our partners ability to enforce our rights under such owned or licensed patents or other intellectual property;

the outcome of ongoing or potential future litigation (and related activities, including inter partes reviews and inter partes reexaminations) or other claims or disputes relating to our business, technologies, products or processes;

our expected revenues (including sales, milestone payments and royalty revenues) from our products or product candidates and any related commercial agreements of ours;

the ability of our manufacturing partners to supply us or our commercial partners with clinical or commercial supplies of our products in a safe, timely and regulatory compliant manner and the ability of such partners to address any regulatory issues that have arisen or may in the future arise;

our ability to retain members of our management team and our employees; and

competition existing today or that will likely arise in the future.

The foregoing does not represent an exhaustive list of risks that may impact the forward-looking statements used herein or in the documents incorporated by reference herein. Please see Risk Factors for additional risks which could adversely impact our business and financial performance and related forward-looking statements.

Moreover, new risks regularly emerge and it is not possible for our management to predict all risks, nor can we assess the impact of all risks on our business or the extent to which any risk, or combination of risks, may cause actual results to differ from those contained in any forward-looking statements. All forward-looking statements included in this Report are based on information available to us on the date hereof. Except to the extent required by applicable laws or rules, we undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise. All subsequent written and oral forward-looking statements attributable to us or persons acting on our behalf are expressly qualified in their entirety by the cautionary statements contained throughout this Report and the documents we have filed with the SEC.

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PART I

Item 1. Description of Business.

Overview

We are a specialty pharmaceutical company that is developing and commercializing, either on our own or in partnerships with third parties, new applications of approved therapeutics to address important unmet medical needs using both proven and new drug delivery technologies. We have developed and are continuing to develop pharmaceutical products aimed principally in the areas of pain management and addiction. We were incorporated in the State of Indiana in 1997 and were reincorporated as a Delaware corporation in 2002.

Our approved products and certain of our product candidates utilize the novel, patent protected and proprietary *BioErodible MucoAdhesive* (or BEMA®) drug delivery technology, a small, erodible polymer film for application to the buccal mucosa (the lining inside the cheek). Our first U.S. Food and Drug Administration (which we refer to as the FDA) approved product, ONSOLIS® (fentanyl buccal soluble film), as well as our approved product BUNAVAIL® (buprenorphine and naloxone buccal film) and our product candidate, BELBUCA (formerly referred to as BEMA® Buprenorphine), utilize our BEMA® technology.

We have worked with other delivery technologies in the past, and as part of our corporate growth strategy, we have licensed, and will continue to seek to acquire or license, additional drug delivery technologies or drugs utilizing the delivery or other technologies of other companies. Clonidine Topical Gel, which we licensed from Arcion Therapeutics (or Arcion) in 2013, and our 2015 agreement with Evonik Corporation (or Evonik) to develop a buprenorphine depot injection formulation, do not utilize the BEMA® technology and allowed us to diversify our portfolio while maintaining a focus in pain and addiction. As we gain access to such technologies, we seek to formulate these technologies with proven, FDA approved therapeutics and utilize our development and commercialization experience to, either by ourselves or through partnerships, navigate the resulting products through the regulatory review process and ultimately bring them to the marketplace.

Our current development strategy focuses primarily on our ability to utilize the FDA s 505(b)(2) approval process to obtain more timely and efficient approval of new formulations of previously approved, active therapeutics incorporated into our drug delivery technology. Because the 505(b)(2) approval process is designed to address new formulations of previously approved drugs, we believe it has the potential to be more cost efficient and expeditious and have less regulatory approval risk than other FDA approval approaches.

An overview of our approved products and key products in development or awaiting approval is set out below:

BELBUCA (BEMA® Buprenorphine) for Chronic Pain

BELBUCA is a partial mu-opioid agonist and a potential treatment for the management of pain severe enough to require daily, around the clock, long-term opioid treatment for which alternative treatment options are inadequate. As described further below, our commercial partner for this product has filed a New Drug Application (or NDA) with the FDA for BELBUCA and we are awaiting the outcome of the FDA s review.

In January 2012, we announced the signing of a worldwide licensing and development agreement for BELBUCA (which we refer to herein as the Endo Agreement) with Endo Pharmaceuticals, Inc. (or Endo) under which we granted to Endo the exclusive, worldwide rights to develop and commercialize BELBUCA for the treatment of chronic pain.

The financial terms of our agreement with Endo include: (i) a $30 million upfront, non-refundable license fee, which we received in January 2012; (ii) $95 million in potential milestone payments based on achievement of pre-defined intellectual property, clinical development and regulatory events (some of which we have received); (iii) $55 million in potential sales threshold payments upon achievement of designated sales levels; and (iv) a tiered, mid- to upper-teen royalty on net sales of BELBUCA in the United States and a mid- to high-single digit royalty on net sales of BELBUCA outside the United States. Endo is one of the premier companies in the area of pain management and has demonstrated significant achievements in the pain space, particularly with the development, launch and commercialization of a portfolio of pain therapeutics including Opana® ER, Lidoderm® and Voltaren® Gel. We believe BELBUCA is an excellent fit with Endo s pain portfolio and will, if approved, add a Schedule III opioid to their branded pain franchise. BELBUCA would complement Endo s pain therapeutics portfolio providing the company with an opportunity to offer a ladder of pain products, aligned with pain severity and opioid scheduling. In particular, BELBUCA would potentially be aligned with the needs of pain specialists and primary care physicians who seek an alternative to Schedule II opioids for the treatment of moderate to severe chronic pain that is not adequately controlled with commonly prescribed first-line therapies (e.g., NSAIDs).

One of the key intellectual property milestones under our Endo Agreement was achieved in February 2012, when the U.S. Patent and Trademark Office (or USPTO) issued a Notice of Allowance regarding one of our patent applications (No. 13/184306) which, once the patent was granted in April 2012, extended the exclusivity of the BEMA® drug delivery technology for BELBUCA (as well as BUNAVAIL®, as discussed below) from 2020 to 2027. As a result, we received a milestone payment from Endo in the

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amount of $15 million in May 2012, and also related to the issuance of the patent, will receive an additional milestone payment of $20 million at the time of approval of a New Drug Application (or NDA) by the FDA for BELBUCA for the treatment of chronic pain. Such amounts are included in the aforementioned $95 million in potential milestone payments based on intellectual property and clinical development and regulatory events.

In May 2012, in close collaboration with Endo, we initiated two Phase 3 clinical studies one in opioid naïve and one in opioid experienced populations. The Phase 3 clinical trials were enriched-enrollment, double-blind, randomized withdrawal studies to evaluate the efficacy and safety of BELBUCA in the treatment of chronic lower back pain in opioid naive and opioid experienced populations. Patients titrated to a well-tolerated, effective dose were randomized to either continue on that dose of BELBUCA , or receive placebo (BEMA® film with no active drug), with treatment continuing for 12 weeks. The primary efficacy endpoint was the mean change in the daily average pain numerical rating scale (NRS-Pain) scores from baseline (just prior to randomization) to week twelve of the double-blind treatment period. Pain was self-reported daily on an 11-point numeric rating scale (daily NRS; 0=no pain, 10=worst possible pain).

Interim analyses were conducted as part of the Phase 3 protocol in both the opioid naïve and opioid experienced studies to allow for adjustments to the sample size in order to maintain appropriate study power to detect statistically significant differences between BELBUCA and placebo. The analyses were conducted by an independent biostatistician. We and Endo announced in September 2013 that, as a result of the interim analyses, no sample size adjustment would be necessary to the opioid naïve study and that additional patients would be added to the ongoing opioid experienced study. The outcomes of the interim analyses were significant because they utilized actual study data to confirm or adjust sample sizes, and importantly, maintain probability of a successful outcome.

On January 23, 2014, we announced with Endo positive top-line results from the Phase 3 efficacy study of BELBUCA in opioid- naïve subjects. The trial successfully met its primary efficacy endpoint in demonstrating that BELBUCA resulted in significantly ($p<0.005$) improved chronic pain relief compared to placebo. Additional secondary endpoints were supportive of the efficacy of BELBUCA compared to placebo. The most commonly reported adverse events in patients treated with BELBUCA compared to placebo were nausea (10% vs. 8%, respectively), vomiting (4% vs. 2%, respectively) and constipation (4% vs. 2%, respectively). The locking of the database for the opioid naïve study triggered a $10 million milestone payment from Endo per the terms of the license agreement, which we received in February 2014.

On July 7, 2014, we announced with Endo positive top-line results from the Phase 3 efficacy study of BELBUCA in opioid- experienced subjects. The trial successfully met its primary efficacy endpoint in demonstrating that BELBUCA resulted in significantly ($p<0.0001$) improved chronic pain relief compared to placebo. Additional secondary endpoints were supportive of the efficacy of BELBUCA compared to placebo. The most commonly reported adverse events in patients treated with BELBUCA compared to placebo were nausea (7.5% vs. 7.4%, respectively) and vomiting (5.5% vs. 2.3%, respectively). Locking of the database for the opioid experienced study triggered an additional $10 million milestone payment from Endo per the terms of the license agreement, which we received July 2014.

On December 23, 2014, we and Endo announced the NDA submission for BELBUCA , which was accepted by FDA in February 2015. Acceptance of the filing of the NDA by FDA triggers an additional $10 million milestone payment from Endo, to be received within 60 days of acceptance. BELBUCA is subject to a ten month FDA review, which could result in an approval in the fourth quarter of 2015 and allow for product launch in early 2016.

BUNAVAIL® (buprenorphine and naloxone) buccal film

We believe that the widespread use of buprenorphine for the treatment of opioid dependence and the need for improved means of delivery to address existing administration challenges present an additional commercial opportunity. Therefore, we developed a BEMA® formulation of buprenorphine and naloxone specifically for the treatment of opioid dependence. The product combines a high dose of buprenorphine along with an abuse deterrent agent, naloxone. BUNAVAIL® provides us with an opportunity to compete in the growing opioid dependence market which, according to Symphony Health, approached $1.8 billion in sales in the U.S in 2014.

In September 2012, we announced the positive outcome of the pivotal pharmacokinetic study comparing BUNAVAIL® to Suboxone® sublingual tablets. The study was designed to compare the relative bioavailability of buprenorphine and naloxone between BUNAVAIL® and the reference product, Suboxone® tablets. The results demonstrated that the two key pharmacokinetic parameters, maximum drug plasma concentration (Cmax) and total drug exposure (AUC), for buprenorphine were comparable to Suboxone® sublingual tablet, and that the same parameters for naloxone were similar or less than Suboxone® tablet. This was followed by initiation of the safety study requested by FDA, assessing the safety and tolerability of BUNAVAIL® in patients converted from a stable dose of Suboxone® (buprenorphine/naloxone) sublingual tablets or films. A total of 249 patients were enrolled in the study, (191 patients completed) which completed in December 2012. Results of the study showed a very favorable safety and tolerability profile along with strong study subject retention and high dose form acceptability ratings. Data showed that over 91% of patients who switched from Suboxone® film or tablets considered the taste of BUNAVAIL® to be very pleasant, pleasant or neutral and over 82%

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rated the ease of use of BUNAVAIL® as very easy, easy or neutral. The study also showed a decrease in the incidence of constipation symptoms from 41% at baseline, before conversion of patients from Suboxone tablets or films to BUNAVAIL®, to 13% following 12 weeks of treatment with BUNAVAIL®.

On July 31, 2013, we submitted the NDA for BUNAVAIL® to the FDA for review, and on June 6, 2014, we announced the FDA approval of BUNAVAIL for the maintenance treatment of opioid dependence as part of a complete treatment plan to include counseling and psychosocial support.

Following thorough review and analysis of a variety of commercialization strategies, which included entertaining commercial partnerships, a decision was made to commercialize BUNAVAIL® utilizing both internal and external resources. In March 2014, we announced we had entered into an agreement with Quintiles to support the launch and commercialization of BUNAVAIL®. Under terms of the agreement, Quintiles provides a range of services to support the commercialization of BUNAVAIL® in the U.S., including recruiting and training a field sales force. Separately, we entered into an agreement with Ashfield Market Access to provide managed markets and trade support for BUNAVAIL®. Ashfield Market Access, which is led by industry veterans including those who led GlaxoSmithKline s managed markets group for more than 20 years, took responsibility for executing a payer strategy aimed at maximizing patient access to BUNAVAIL®.

On November 3, 2014, we announced the availability of BUNAVAIL® in the U.S. where it is being supported by a 60-person field sales force and a full marketing effort targeting the nearly 5,000 physicians who are responsible for approximately 90% of prescriptions for buprenorphine products for the treatment of opioid dependence, according to Symphony Health.

ONSOLIS® (fentanyl buccal soluble film)

On July 16, 2009, we announced the U.S. approval of our first product, ONSOLIS® (fentanyl buccal soluble film). ONSOLIS® is indicated for the treatment of breakthrough pain (i.e., pain that breaks through the effects of other medications being used to control persistent pain) in opioid tolerant patients with cancer. In May 2010, regulatory approvals were granted for Canada, and in October 2010, approval was obtained in the European Union (which we refer to herein as E.U.) through the E.U. s Decentralized Procedure, with Germany acting as the reference member state. ONSOLIS® is marketed in Europe under the trade-name BREAKYL .

The FDA approval of ONSOLIS®, together with our satisfactory preparation of launch supplies of ONSOLIS®, triggered the payment to us by our commercial partner, Meda AB, a leading international specialty pharmaceutical company based in Sweden (which we refer to herein as Meda), of approval milestones aggregating $26.8 million. The first national approval of BREAKYL in the E.U. resulted in a milestone payment of $2.5 million from Meda. A second milestone payment of $2.5 million was subsequently realized at the time of first commercial sale in the E.U. in October 2012. We began receiving royalties from Meda on net sales of ONSOLIS® in the U.S. and Canada following launch and from BREAKYL following launch in the E.U. Our royalty revenue from this product remains below original projections due to certain regulatory conditions in the U.S., which are discussed below.

We granted commercialization and distribution rights for ONSOLIS® on a worldwide basis (except in South Korea and Taiwan) to Meda. Meda s U.S. subsidiary, Meda Pharmaceuticals, based in Somerset, New Jersey, is a specialty pharmaceutical company that develops, markets and sells branded prescription therapeutics. Meda secured access to additional markets through acquisition of European businesses from Valeant Pharmaceuticals International, Inc., which we refer to herein as Valeant and a joint venture with Valeant covering Australia, Mexico and Canada.

In 2010, we secured commercialization rights for ONSOLIS® for the remaining worldwide territories through execution of licensing agreements with KUNWHA Pharmaceutical Co., Ltd. (or Kunwha), for South Korea and TTY Biopharm Co., Ltd. (or TTY) for Taiwan where the product will be marketed as PAINKYL .

Although we have generated licensing-related and other revenue to date from the commercial sales of an approved product ONSOLIS®/BREAKYL such revenue has been minimal to date due to multiple factors, including a highly restrictive Risk Evaluation and Mitigation Strategy (REMS) imposed by the FDA and certain formulation issues described below. The lack of approved REMS programs for our direct competitors resulted in an un-level playing field, which created an unfavorable selling environment for ONSOLIS® into 2012. In the E.U., BREAKYL began to be launched on a country by country basis starting in the fourth quarter of 2012.

On December 29, 2011, the FDA approved a class-wide REMS program covering all transmucosal fentanyl products under a single risk management program. The program, which is referred to as the Transmucosal Immediate Release Fentanyl (TIRF) REMS Access Program, was designed to ensure informed risk-benefit decisions before initiating treatment with a transmucosal fentanyl product, and while patients are on treatment, to ensure appropriate use. The TIRF REMS program was implemented in March 2012. The approved program covers all marketed transmucosal fentanyl products under a single program which will enhance patient safety while limiting the potential administrative burden on prescribers and their patients. One common program also ended the disparity in prescribing requirements for ONSOLIS® compared to similar products and provided ONSOLIS® with the opportunity for retail and inpatient facility access.

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On March 12, 2012, we announced the postponement of the U.S. re-launch of ONSOLIS® following the initiation of the class-wide REMS until the product formulation could be modified to address two appearance-related issues. Such appearance-related issues involved the formation of microscopic crystals and a fading of the color in the mucoadhesive layer, raised by the FDA during an inspection of our North American manufacturing partner for ONSOLIS®, Aveva Drug Delivery Systems, Inc. (or Aveva). While the appearance issues do not affect the product s underlying integrity, safety or performance, the FDA believes that the fading of the color in particular may potentially confuse patients, necessitating a modification of the product and its specification before it can be manufactured and distributed. The source of microcrystal formation and the potential for fading of ONSOLIS® was found to be specific to a buffer used in its formulation. We modified the formulation and as of the date of this report have 12 months of stability data on the reformulated product that shows no signs of microcrystal formation or color changes.

On January 27, 2015, we announced that we had entered into an assignment and revenue sharing agreement with Meda to return back to us the marketing authorizations for ONSOLIS® for the U.S. and the right to seek marketing authorizations for ONSOLIS® in Canada and Mexico. Once the NDA has been returned, we will have the right to work directly with the FDA and submit a prior approval supplement that responds to FDA questions and requests and will hopefully lead to the re-introduction of the product. FDA s review of the application may take up to 6 months; therefore, it is possible to have a decision before the end of 2015.

Clonidine Topical Gel

In March 2013, we announced our entry into a worldwide Exclusive License Agreement (which we refer to as the Arcion Agreement) with privately held Arcion, under which we will develop and commercialize Clonidine Topical Gel (formerly ARC4558) for the treatment of painful diabetic neuropathy (or PDN) and potentially other indications. Under the terms of the agreement, we made an upfront payment of $2 million to Arcion in the form of unregistered shares of our common stock. Additional financial terms of the licensing agreement include a milestone payment to Arcion of $2.5 million in unregistered shares of our common stock upon acceptance by the FDA of a NDA for Clonidine Topical Gel and a cash payment to Arcion of between $17.5 and $35 million upon NDA approval, depending on certain regulatory and commercial considerations. In addition, the licensing agreement includes sales milestones and low single-digit royalties on net worldwide sales.

We believe that the PDN market is highly under-served by existing products and therefore there is a strong scientific rationale for developing a topical treatment for PDN that delivers analgesia in a way that avoids systemic side effects. Evidence has shown that clonidine stimulates an inhibitory receptor in the skin associated with pain fibers. Arcion has assessed its effectiveness in reducing pain in PDN in a double-blind, placebo-controlled, Phase 2 study where the primary study endpoint was the change in pain intensity over a 3 month treatment period in diabetic foot pain. A significant treatment difference was seen in the planned subset analysis of diabetic patients who had documented evidence of functioning pain receptors in the skin of the lower leg (p=0.01, n=63) thus, at a minimum, supporting the effectiveness of topical clonidine in diabetic patients with functioning pain receptors of the skin. In the overall population that included patients without functioning nerve receptors , there was a trend favoring topical Clonidine Topical Gel (p=0.07, n= 182), though the overall results did not reach statistical significance.

Oral medications that are approved for the treatment of PDN include anticonvulsants such as Lyrica (pregabalin), the antidepressant Cymbalta® (duloxetine) and the opioid Nucynta® ER (tapentadol ER), with sales for the treatment of neuropathic pain totaling over $3 billion in the U.S. according to Datamonitor. These treatments are modestly effective in relieving symptoms and their use can be limited by adverse effects and drug interactions.

We met with representatives of the FDA on November 21, 2013 to discuss the development program for Clonidine Topical Gel for the treatment of PDN. The FDA agreed with the proposed clinical program which included two

placebo-controlled studies and one long term safety study in patients suffering from painful diabetic neuropathy, the number of treated subjects required for the safety assessment and the plan for data integration of previously performed and planned clinical studies. The discussion provided us with the input and clarity needed to move the program directly to Phase 3. It also appears that the FDA recognizes the need for new treatment options for PDN by confirming Fast Track designation for the program that could potentially lead to a priority review.

In early April 2014, we announced enrollment of the first patient in the Phase 3 clinical study of Clonidine Topical Gel for PDN, and in early August 2014, we announced that we completed a pre-specified interim analysis of the study. The interim analysis was performed on data from the first 50% of patients who completed the study. The purpose of the interim analysis was to allow for a sample size adjustment if necessary to maintain appropriate statistical power to detect a treatment effect between Clonidine Topical Gel and placebo. As a result of the interim analysis, a total of approximately 80 additional patients were to be added to the trial in an effort to maintain 90% percent power to detect a statistically significant difference between Clonidine Topical Gel and placebo. The analysis was conducted by an independent biostatistician.

If the initial placebo controlled study meets its primary endpoint, the results for which are anticipated to be available by the end of the first quarter of 2015, and we initiate the second placebo controlled study in early 2015, we could be in a position to submit an NDA in 2016.

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Buprenorphine Depot Injection

In 2014, we entered into an exclusive agreement with Evonik to develop and commercialize a proprietary, injectable microparticle formulation of buprenorphine potentially capable of providing 30 days of continuous therapy following a single subcutaneous injection. Microsphere-based, long acting, buprenorphine injectable depot has the ability to change the treatment paradigm in opioid dependence. Such a dosage form has the opportunity to improve therapy compliance through continuous delivery of drug for up to 30 days and addresses challenges regarding patient adherence to long-term buprenorphine treatment, which is critical to successfully manage opioid dependence and the potential for misuse and diversion.

While we plan to pursue an indication for the maintenance treatment of opioid dependence, we have also secured the rights and plans to develop a product for the treatment of chronic pain in patients requiring continuous opioid therapy. As part of the agreement, we will have the right to license the product(s) following the attainment of Phase 1 ready formulations. At that point, Evonik could receive downstream payments for milestones related to regulatory filings and subsequent NDA approvals as well as product royalties. Evonik has the exclusive rights to develop the formulation and manufacture the product(s).

We plan to submit an Investigational New Drug application (or IND) for this product candidate to FDA in the second half of 2015.

Additional Overview Information

From our inception through December 31, 2014, we have recorded accumulated losses totaling approximately $205.5 million. Our historical operating losses have resulted principally from our research and development activities, including clinical trial activities for our product candidates and general and administrative expenses. Ultimately, if we secure additional approvals from the FDA and other regulatory bodies throughout the world for our product candidates, our goal will be to augment our current sources of revenue and, as applicable, deferred revenue (principally licensing fees), with sales of such products or royalties from such sales, on which we may pay royalties or other fees to our licensors and/or third-party collaborators as applicable.

We intend to finance our research and development, commercialization and distribution efforts and our working capital needs primarily through:

- commercializing our approved products such as BUNAVAIL®;
- partnering with other pharmaceutical companies such as Meda and Endo to assist in the distribution of our products like ONSOLIS® and BELBUCA , for which we would expect to receive an upfront payment, milestones and royalty payments; and
- securing proceeds from public and private financings and other strategic transactions.

We have based our estimates of development costs, market size estimates, peak annual sales projections and similar matters described below and elsewhere in this Report on our market research, third party reports and publicly available information which we consider reliable. However, readers are advised that the projected dates for filing and approval of our INDs or NDAs with the FDA or other regulatory authorities, our estimates of development costs, our

projected sales and similar metrics regarding BUNAVAIL®, ONSOLIS®, BELBUCA , Clonidine Topical Gel, Buprenorphine Depot Injection or any other product candidates discussed below and elsewhere in this Report are merely estimates and subject to many factors, many of which may be beyond our control, which will likely cause us to revise such estimates. Readers are also advised that our projected sales figures do not take into account the royalties and other payments we will need to make to our licensors and strategic partners. Our estimates are based upon our management s reasonable judgments given the information available and their previous experiences, although such estimates may not prove to be accurate.

The BEMA® Drug Delivery Technology

Our BEMA® drug delivery technology consists of a small, bi-layered erodible polymer film for application to the buccal mucosa (the lining inside the cheek). BEMA® films have the capability to deliver a rapid, reliable dose of drug across the buccal mucosa for time-critical conditions such as breakthrough cancer pain or in situations where gastrointestinal absorption of an oral drug is not practical or reliable, or in facilitating the administration of drugs with poor oral bioavailability.

We believe that the BEMA® technology permits control of two critical factors allowing for better dose-to-dose reproducibility: (i) the contact area for mucosal drug delivery, and (ii) the time the drug is in contact with that area, known as residence time. In contrast to competing transmucosal delivery systems like lozenges, buccal tablets and matrix-based delivery systems placed under the tongue or sprayed in the oral cavity, BEMA® products are designed to:

- adhere to buccal mucosa in seconds and dissolve in minutes;

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permit absorption without patients being required to move the product around in the mouth for absorption, thus avoiding patient intervariability;

provide a reproducible delivery rate, not susceptible to varying or intermittent contact with oral membranes; and

dissolve completely, leaving no residual product or waste and avoiding patient removal, and the possibility for diversion or disposal of partially used product.

We currently own the BEMA® drug delivery technology. We previously licensed the BEMA® drug delivery technology on an exclusive basis from Atrix Laboratories (previously known as QLT USA, Inc., now known as TOLMAR Therapeutics, Inc., which we refer to herein as Tolmar).

Overview of Specialty Pharmaceuticals and the 505(b)(2) Regulatory Pathway

Our corporate focus is specialty pharmaceuticals with characteristics that provide substantial points of differentiation from existing products. Our product portfolio is based on the application of drug delivery technologies and/or new dosage forms/indications to existing drugs for the creation of novel products. We then seek proprietary protection and FDA approval, and subsequently commercialize these products ourselves or through partners. We believe that research and development efforts focused on novel dose forms of FDA approved drugs is less risky than attempting to discover new drugs, sometimes called new chemical entities (known as NCEs). Our corporate focus came to initial fruition with the FDA s approval of ONSOLIS® (fentanyl buccal soluble film) in 2009 and was replicated in 2014 with the approval of BUNAVAIL® (buprenorphine/naloxone buccal film). It is our goal to replicate this success with our current product candidates, and to identify new product candidates suitable for this development strategy that would add significant commercial value to us.

An important part of our strategy is the utilization of FDA s 505(b)(2) NDA process for approval. Under the 505(b)(2) process, we are able to seek FDA approval of a new dosage form, dosage regimen or new indication of an FDA approved drug . This regulation enables us to partially rely on the FDA s previous findings of safety and effectiveness for the drug, including clinical and nonclinical testing, and thereby reduce, although not eliminate, the need to engage in these costly and time consuming activities. A typical development program for a 505(b)(2) submission will include:

seven, 14 or 28-day multiple dose toxicity studies in a single species of animals,

pharmacokinetic evaluation of the new dosage form in humans,

stability data of the drug substance,

description of drug product components,

description and validation of manufacturing process,

one year stability data on three commercial scale batches of drug product, and

depending on the drug product, may include:

(i) one or more placebo controlled clinical studies in humans to establish the efficacy of the product, and/or

(ii) a long term clinical study to establish the safety of the product in the intended patient population.

This drug development and regulatory approval process is less extensive and lengthy than for a NCE and, as a result, we believe, is a more cost effective way to bring new product candidates to market.

We have and intend to continue to target drugs that have established markets and an opportunity to introduce a new form of delivery of that product in order to meet an unmet market need. As a result of employing well known drugs in novel technologies or new dosage forms/indications, we believe health care providers will be familiar with the drugs and accustomed to prescribing them. As with ONSOLIS®, BELBUCA , BUNAVAIL® and Clonidine Topical Gel, our drug candidates have been through the regulatory process with safety and efficacy established for an indication, a formulation and a dose range. Consequently, our clinical trials need to demonstrate the safety and efficacy of our products in the chosen patient population.

Endo Licensing Agreement for BELBUCA (BEMA® Buprenorphine)

On January 6, 2012, we announced the signing of a world-wide licensing and development agreement for BELBUCA with Endo. Under terms of the agreement, Endo will be responsible for the manufacturing, distribution, marketing and sales of BELBUCA on a worldwide basis. Endo will commercialize BELBUCA outside the U.S. through its own efforts or through regional partnerships. In the U.S., both companies will collaborate on the planning and finalization of the Phase 3 clinical development program and regulatory strategy for BELBUCA for chronic pain. We will maintain responsibility for the conduct of planned clinical studies leading up to the submission of the NDA. Endo will have the responsibility of submitting the NDA and managing the interactions with the FDA.

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In aggregate, the agreement is worth up to $180 million to us if all milestones or thresholds are met, which includes an upfront non-refundable license fee of $30 million (received January 2012), as well as intellectual property, development, regulatory and commercial milestone and sales threshold payments. Additionally, we will receive a tiered mid to upper teen royalty on U.S. net sales of BELBUCA and a tiered mid to upper single-digit royalty on sales outside the U.S. One of the key intellectual property milestones under our Endo Agreement was achieved when, in April 2012, the USPTO granted US Patent No. 8,147,866 (issued from US Patent Application No. 13/184,306), which will extend the exclusivity of the BEMA® drug delivery technology for BELBUCA (as well as BUNAVAIL® discussed below) from 2020 to 2027. As a result (and included in the aforementioned $180 million if all milestones or thresholds are met), we received a milestone payment in the amount of $15 million in May 2012, and have become eligible for an additional milestone payment of $20 million which will be paid at the time of approval of a NDA by the FDA for BELBUCA . Additionally, we achieved another milestone with the locking of the database for our Phase 3 opioid naive clinical study on January 17, 2014. For the achievement of this milestone, per the terms of the agreement, we were due a milestone payment in the amount of $10 million, which was received February 2014 (which is included in the aforementioned $180 million if all milestones or thresholds are met) within thirty (30) days of the database lock. On June 25, 2014, the database for the pivotal Phase 3 efficacy study of BELBUCA in opioid-experienced patients was locked. The locking of the database triggered a $10 million milestone payment from Endo, which was received July 2014. On December 23, 2014, we and Endo announced the submission of a NDA for BELBUCA to the FDA, which was accepted February 23, 2015, which triggers a $10 million milestone payment due from Endo to us.

Meda Licensing Agreements for ONSOLIS®

North American Agreement. On September 5, 2007, we entered into a definitive License and Development Agreement with Meda and our subsidiary Arius pursuant to which we and Arius agreed to grant to Meda an exclusive commercial license to market, sell, and, following regulatory approval, continue development of ONSOLIS® in the United States, Mexico and Canada (which we refer to as the Meda North American License).

Pursuant to such license agreement, we have received or will receive:

a $30.0 million milestone payment (received in 2007).

a $29.8 million milestone payment for the approval of ONSOLIS® by the FDA and provision of commercial supplies of ONSOLIS® in the U.S. (received in 2009).

a double digit royalty on net sales of ONSOLIS® in the covered territories, subject to certain third party royalty payment costs and adjustments, as well as other adjustments in the event of certain specific supply disruptions. The license agreement provides for certain guaranteed minimum annual royalties to us during the second through seventh years following the product s first commercial sale, which occurred in the fourth quarter of 2009.

sales milestones equaling an aggregate of $30 million will be payable at:

$10.0 million when and if annual sales meet or exceed $75.0 million;

$10.0 million when and if annual sales meet or exceed $125.0 million; and

$10.0 million when and if annual sales meet or exceed $175.0 million.

Also, pursuant to the Meda North American License, we have been granted certain rights to co-promote ONSOLIS® using our own sales force, with financial support by Meda for such efforts. In addition, Meda is subject to certain minimum sales representative calls and advertising and promotional expenditure requirements under the North American license agreement and has agreed to support all future costs of clinical development, such as additional indications for ONSOLIS® that do not involve studies in support of the NDA.

European Agreement. In 2006, we announced collaboration with Meda to develop and commercialize BEMA® Fentanyl (marketed as BREAKYL in Europe). Under terms of the agreement, we granted Meda rights to the European development and commercialization of BREAKYL , in exchange for an upfront fee of $2.5 million and a $2.5 million milestone payment (received in 2008) for completion of Phase 3 clinical trials. We have also received a double digit royalty on net sales and additional milestone payments of $2.5 million upon approval and $2.5 million upon launch in the first country in the European territory (received in 2012). Meda has managed the regulatory submission in Europe that led to approval in October 2010. Meda will exclusively commercialize BREAKYL in Europe.

In 2009, we received a $3 million payment in exchange for amending the European agreement to provide Meda the worldwide rights to ONSOLIS®, with the exception of Korea and Taiwan. The sales royalties to be received by us will be the same for all territories as agreed to for Europe. In addition, various terms of the European agreements have been modified to reflect the rights and obligations of both us and Meda in recognition of the expansion of the scope of the European agreements.

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Assignment and Revenue Sharing Agreement. On January 23, 2015, we entered into an assignment and revenue sharing agreement with Meda (which we refer to as the Assignment Agreement), under which Meda will transfer back to us the marketing authorizations for ONSOLIS® for the United States and the right to seek marketing authorizations for ONSOLIS® in Canada and Mexico.

Under the Assignment Agreement, for a period of up to approximately one year, we shall have the right and shall use commercially reasonable efforts to work directly with the FDA to attempt to resolve certain previously disclosed issues relating to ONSOLIS® in the United States and seek, and attempt to negotiate a definitive license agreement with, one or more new commercial partners for ONSOLIS® in the United States, Canada and Mexico (each a Subject Country and collectively, the Subject Countries) (such an agreement, a Replacement License and such a partner, a Replacement Licensee).

Following the effective date of the Assignment Agreement, Meda s rights and obligations related to the development and commercialization of ONSOLIS® in the Subject Countries shall be suspended. Prior to the entry by us into a Replacement License, we and Meda will negotiate in good faith a form of definitive termination agreement addressing in further detail the termination of the Meda North American License and its effects (which we refer to as the Termination Agreement). Pursuant to the Assignment Agreement, any Termination Agreement is required to include provisions requiring us to share with Meda various percentages of revenue received by the Company under any Replacement License for ONSOLIS® after, subject to certain limitations, first deducting from such revenue payments required to be made by us under that certain Clinical Development and License Agreement, dated July 14, 2005, as amended, between the us, our subsidiary, Arius Two, Inc., and CDC V, LLC.

In the event that we have not identified a Replacement Licensee and entered into a Replacement License by a certain agreed upon date, Meda will have the right, but not the obligation, to demand that the marketing authorizations, and the rights to pursue marketing authorizations, for ONSOLIS® in the Subject Countries revert back to Meda, with the full reinstatement of all of Meda s rights and obligations under the Meda North American License. Notwithstanding the foregoing, Meda s rights to terminate the Meda North American License remain unaffected by the Assignment Agreement. Subject to any such reversion of rights back to Meda or earlier termination, the Assignment Agreement shall terminate on the earlier of (i) the termination of the Meda North American License or (ii) on February 28, 2016 without Meda s exercising its right to cause reactivation or our execution of a Replacement License with a Replacement Licensee.

Key Collaborative and Supply Relationships

We are and have been a party to collaborative agreements with corporate partners, contractors, universities and government agencies. Research collaboration may result in new inventions which are generally considered joint intellectual property unless invented solely by individuals we employ, or by third party transfer to us by contract. Our collaboration arrangements are intended to provide us with access to greater resources and scientific expertise in addition to our in-house capabilities. We also have supply arrangements with several of the key component producers of our delivery technology. Our collaborative and supply relationships include:

Endo. We believe that our agreement with Endo is currently one of our most important third party agreements. For a description of our agreements with Endo, please see Endo Pharmaceutical Licensing Agreement for BELBUCA above.

Meda. We believe that our agreements with Meda are currently one of our most important third party agreements. For a description of our agreements with Meda, please see Meda Licensing Agreements for ONSOLIS® above.

Aveva Drug Delivery Systems. Effective October 17, 2005, we entered into an agreement with Aveva pursuant to which Aveva acts as our North American supplier of ONSOLIS® for clinical trials and commercial sale. Under the terms of this agreement, Aveva will be the sole supplier of ONSOLIS® for the United States, Mexico and Canada.

Our supply agreement with Aveva runs for a term of four years from the first commercial sale of ONSOLIS® (October 2009) and can be renewed for subsequent two year terms. Either we or Aveva can terminate the agreement on advanced written notice. On October 9, 2014, Aveva sent us written notice of their intent not to renew our supply agreement. Therefore, our supply agreement with Aveva will expire on October 15, 2015. We will seek alternative manufacturing arrangements for ONSOLIS® in the U.S. in the event we are able to secure a new commercial partner for the product.

On March 12, 2012, we announced the postponement of the U.S. re-launch of ONSOLIS® following the initiation of the class-wide REMS until the product formulation could be modified to address two appearance-related issues. Such appearance-related issues involved the formation of microscopic crystals and a fading of the color in the mucoadhesive layer, raised by the FDA during an inspection of our North American manufacturing partner for ONSOLIS®, Aveva. While the appearance issues do not affect the product s underlying integrity, safety or performance, the FDA believes that the fading of the color in particular may potentially confuse patients, necessitating a modification of the product and its specification before it can be manufactured and distributed. The source of microcrystal formation and the potential for fading of ONSOLIS® was found to be specific to a buffer used in its formulation. We modified the formulation and as of the date of this report have 12 months of stability data on the reformulated product that shows no signs of microcrystal formation or color changes.

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LTS Lohmann Therapie-Systeme AG. Effective December 15, 2006, we entered into a Process Development Agreement with LTS Lohmann Therapie-Systeme AG (which we refer to herein as LTS), pursuant to which LTS will undertake process development, scale-up activities and supply BREAKYL to us for European clinical trials. Under the agreement, LTS has granted us a license under European Patent No. 0 949 925, in regard to BREAKYL in the E.U.

On September 13, 2012, we executed a Manufacturing, Supply, and License Agreement, effective April 26, 2012, with LTS, under which LTS will manufacture and supply us our BREAKYL product for distribution outside of the U.S. and Canada. We are required to supply BREAKYL product to Meda, Kunwha, and TTY pursuant to our obligations under certain license and supply agreements under which Meda, Kunwha, and TTY develop and commercialize the BREAKYL product. In conjunction with the agreement, LTS has waived all royalties on products that they produce. This does not preclude royalties that we owe to LTS if we produce BREAKYL with another company.

ARx. Effective July 30, 2014, we entered into an agreement with ARx, LLC. Pursuant to which ARx acts as a supplier of BUNAVAIL® laminate or bulk product for the United States. Our supply agreement with ARx runs for a term from July 30, 2014 until December 31, 2019 and can be renewed for additional terms by mutual agreement.

Sharp. Effective March 6, 2014, we entered into an agreement with Sharp Corporation to punch or cut the BUNAVAIL® laminate or bulk product into individual dosage units and package them to supply the finished BUNAVAIL® film products. Our supply agreement with Sharp runs for an initial term from March 6, 2014 until December 31, 2016 and can be extended by mutual agreement for subsequent one year terms.

Quintiles. In March 2014, we announced we had entered into an agreement with Quintiles to support the launch of BUNAVAIL®. Under terms of the agreement, Quintiles provides a range of services to support the commercialization of BUNAVAIL® in the U.S., including recruiting and training a field sales force. Our agreement with Quintiles shall continue until terminated, and the agreement is terminable upon notice by either party and also in cases of breach of the agreement by either party.

We also have relationships with third party contract research organizations that assist us with the management of our clinical trials.

In pursuing potential commercial opportunities, we intend to seek and rely upon additional collaborative relationships with corporate partners. Such relationships may include initial funding, milestone payments, licensing payments, royalties, access to proprietary drugs or potential applications of our drug delivery technologies or other relationships. Our agreements with Endo and Meda are examples of these types of relationships, and we will continue to seek other similar arrangements.

Relationship with CDC IV, LLC

On July 14, 2005, we entered into a Clinical Development and License Agreement (which we refer to as the CDLA), with the predecessor of CDC IV, LLC (which we refer to herein as CDC), which provided funds to us for the development of ONSOLIS®. On February 16, 2006, we announced that, as a result of our achievement of certain milestones called for under the CDLA, CDC made its initial $2 million payment to us. On May 16, 2006, we issued CDC 2 million shares of our common stock in return for accelerating the funding of the $4.2 million balance of $7

million of aggregate commitment under the CDLA and for eliminating the then required $7 million milestone repayment to CDC upon the approval by the FDA of ONSOLIS®.

Under the CDLA, as amended, CDC is entitled to receive a low-double digit royalty based on net sales of ONSOLIS®. The CDLA includes minimum royalties of $375,000 per quarter beginning in the second full year following commercial launch. The minimum provision came into effect in 2011. The royalty term and minimum payments end upon the latter of expiration of the patent or generic entry into any particular country.

The term of the CDLA lasts until the CDLA is terminated. Either we or CDC may terminate the CDLA for uncured breach or upon bankruptcy-like events, in each case following written notice. CDC may terminate the CDLA, following applicable cure periods, if we: (i) default on indebtedness in excess of $1 million which was accelerated or for which payment has been demanded, or (ii) fail to satisfy a judgment greater than $500,000.

During 2006 and 2007, we were a party to disputes with CDC. On September 5, 2007, in connection with CDC s consent to the Meda North American licensing transaction, we and CDC entered into a Dispute Resolution Agreement (or DRA) pursuant to which we and CDC agreed to waive and dismiss with prejudice all current disputes between us and CDC. As a condition to CDC s entry into

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the DRA and its consent to the Meda North American licensing transaction, we and CDC entered into a Royalty Purchase and Amendment Agreement, dated September 5, 2007 (or the RPAA) pursuant to which: (i) we granted CDC a right of first refusal on our financings, which replaced a right of first negotiation on financings previously held by CDC (which we refer to as the ROFR) and (ii) we granted CDC a 1% royalty on sales of the next BEMA® product, which will be BUNAVAIL®, including an active pharmaceutical ingredient other than fentanyl, to receive FDA approval. The ROFR terminated in accordance with its terms as of February 28, 2014 because, as provided for in the RPAA, we maintained a volume weighted average stock price of $9.00 per share for ten (10) trading days during any twenty (20) consecutive trading day period.

In connection with the 1% royalty grant as previously mentioned: (i) CDC shall have the option to exchange its royalty rights to BUNAVAIL® in favor of royalty rights to a substitute BEMA® product, (ii) we shall have the right, no earlier than six (6) months prior to the initial commercial launch of BUNAVAIL®, to propose in writing and negotiate the key terms pursuant to which it would repurchase the royalty from CDC, (iii) CDC s right to the royalty shall immediately terminate at any time if annual net sales of BUNAVAIL® equal less than $7.5 million in any calendar year following the third (3rd) anniversary of initial launch of the product and CDC receives $18,750 in three (3) consecutive quarters as payment for CDC s 1% royalty during such calendar year and (iv) CDC shall have certain information rights with respect to BUNAVAIL®. The amount of royalties which we may be required to pay (including estimates of the minimum royalties) is not presently determinable because product sales estimates cannot be reasonably determined and the regulatory approvals of the product for sale is not possible to predict. As such, we expect to record such royalties, if any, as cost of sales.

On May 12, 2011, we entered into an Amendment to the CDLA with CDC and NB Athyrium LLC (or Athyrium). Under the terms of the CDLA Amendment, among other matters, the parties agreed to increase the royalty rate to be received by CDC/Athyrium retroactively to the initial launch date of ONSOLIS® and, accordingly, we recorded $0.3 million as additional cost of product royalties for the year ended December 31, 2011. In addition, certain terms of the CLDA were amended and restated to clarify that royalty payments by us under the CDLA will be calculated based on Meda s sales of ONSOLIS®, whereas previous royalty payments by us to CDC were calculated based on sales of ONSOLIS® by us to Meda. The difference between these two calculations resulted in a $1.1 million overpayment by us which was recorded as a prepayment. As a result, we did not pay any of the quarterly royalty payments (including any 2011 payments) due to CDC/Athyrium until the December 31, 2011 royalty calculation, which we paid during the first quarter of 2012

Research and Development

The significant majority of our research and development relating to our BEMA® technology is conducted through third parties in collaboration with us.

Research and development expenses include salaries and benefits for personnel involved in our research and development activities and direct and third party development costs, which include costs relating to the formulation and manufacturing of our product candidates, costs relating to non-clinical studies, including toxicology studies, and clinical trials, and costs relating to compliance with regulatory requirements applicable to the development of our product candidates. For the years ended December 31, 2014, 2013 and 2012, we spent approximately $34.3 million, $53.3 million and $35.4 million, respectively, on research and development, and such expenses represented approximately 47%, 81% and 78%, respectively, of our total operating expenses for such fiscal years.

Endo is responsible for reimbursing us for certain research and development clinical trial expenses that exceed $45 million, as detailed in our License and Development Agreement that was executed on January 5, 2012. For the years ended December 31, 2014 and 2013, we have incurred $12.7 million and $2.8 million, respectively, in such research

and development expenses that are reimbursable by Endo to us. These reimbursable expenses are the primary activity within the reimbursable revenue account in the accompanying consolidated statement of operations as of December 31, 2014 and 2013.

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Market Overview for ONSOLIS®, BELBUCA , BUNAVAIL® and Our Product Candidates

The following table summarizes the status of our marketed product and our current product candidates and product concepts:

Product/Formulation	Indication	Development Status	Commercial Status
ONSOLIS®/BREAKYL / PAINKYL (U.S./E.U./Taiwan trade names, respectively)	Breakthrough cancer pain in opioid tolerant patients	Approval: U.S. in July 2009; Canada in May 2010; E.U. in October 2010 and Taiwan in July 2013	Partnered outside the U.S., Canada and Mexico
BELBUCA	Moderate to severe chronic pain	NDA accepted February 2015	Partnered worldwide with Endo
BUNAVAIL®	Treatment of opioid dependence	Approval: June 2014	In-house commercialization
Clonidine Topical Gel	Treatment of painful diabetic neuropathy	Phase 3 program in process	In-house commercialization for specialty indications possible; primary care rights expected to be partnered
Buprenorphine Depot Injection	Opioid dependence and chronic pain	IND submission anticipated in late 2015	Not partnered

The pharmaceutical industry and the therapeutic areas in which we compete are highly competitive and subject to rapid and substantial regulatory and technological changes. Developments by others may render our BEMA® technology, our marketed products and any proposed drug products and formulations under development noncompetitive or obsolete, or we may be unable to keep pace with technological developments or other market factors. Technological competition in the industry from pharmaceutical and biotechnology companies, universities, governmental entities and others diversifying into the field is intense and is expected to increase.

Below are some examples of companies seeking to develop potentially competitive technologies, though the examples are not all-inclusive. Many of these entities have significantly greater research and development capabilities than do we, as well as substantially more sales and marketing, manufacturing, financial and managerial resources. These entities represent significant competition for us. In addition, acquisitions of, or investments in, competing pharmaceutical or biotechnology companies by large corporations could increase such competitors research, financial, sales and marketing, manufacturing and other resources. Such potential competitive technologies may ultimately prove to be safer, more effective, or less costly than any product candidates that we are currently developing or may be able to develop. Additionally, our competitive position may be materially affected by our ability to develop or successfully commercialize our drugs and technologies before any such competitor. Other external factors may also impact the ability of our products to meet expectations or effectively compete, including pricing pressures, healthcare reform and other government interventions as well as limitations on access that may be placed upon us through managed care organizations or through competitive contracting with payers.

There have been a growing number of companies developing products utilizing various thin film drug delivery technologies. While numerous over-the-counter pharmaceutical products have been brought to market in thin film formulations, few containing prescription products have been introduced in the U.S. Among the products to receive FDA approval are ONSOLIS® and BUNAVAIL® (BDSI), Suboxone® film (Indivior) and Zuplenz® (Galena). Leading companies in the development and manufacture of thin film technologies include LTS, ARx LLC and MonoSol Rx LLC (or MonoSol). In addition, a number of companies are developing improved versions of existing products using oral dissolving, nasal spray, aerosol, sustained release injection and other drug delivery technologies. We believe that potential competitors are seeking to develop and commercialize technologies for buccal, sublingual or mucosal delivery of various therapeutics or groups of therapeutics. While our information concerning these competitors and their development strategy is limited, we believe our technology can be differentiated because the BEMA® technology provides for a rapid and consistent delivery, high drug bioavailability and convenient use based on how the BEMA® technology adheres to the buccal membrane and dissolves. Our clinical trials across a number of BEMA® products have demonstrated that the technology is an effective means of drug delivery that is well tolerated and offers convenience to patients.

ONSOLIS®

According to the National Cancer Institute, there are approximately 12.5 million people in the United States diagnosed with or living with cancer. Cancer patients often suffer from a variety of symptoms including pain as a result of their cancer or cancer treatment. Pain is a widely prevalent symptom in cancer patients, and an estimated 50% to 90% of those with cancer also suffer from what is referred to as breakthrough cancer pain or BTCP . Following rapid onset that peaks in three to five minutes, BTCP episodes

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can last several minutes to an hour, and usually occur several times per day. BTCP can be difficult to treat due to its severity, rapid onset and the often unpredictable nature. Physicians typically treat BTCP with a variety of short-acting opioid medications, including morphine and fentanyl. A number of formulations of fentanyl are available employing a variety of drug delivery technologies, all which provide rapid onset and relatively short duration of action to address the fast onset and short duration of BTCP.

For ONSOLIS®, in the breakthrough cancer pain area, the market has become increasingly crowded and more competitive in recent years. The principal competitor has traditionally been Teva Pharmaceutical Industries Ltd. (NASDAQ:TEVA), which completed its acquisition of Cephalon, Inc. in October 2011. Teva markets both lozenge (Actiq®) and effervescent buccal tablet (Fentora®) formulations of fentanyl. Over the last year, newer products entries, particularly Subsys® (fentanyl sublingual spray) from Insys) have gained significant market share. Additional competitors include Galena Biopharma which licensed from Orexo and subsequently relaunched the sublingual tablet formulation of fentanyl (Abstral®) and DepoMed, which licensed a nasal spray formulation of fentanyl (Lazanda®) from Archimedes. In addition, multiple generic formulations of Actiq® are currently available.

The transmucosal fentanyl class has faced significant challenges following safety issues stemming from inappropriate use of Fentora® and the subsequent Dear Doctor letter (Cephalon Press Release, September 2007). Furthermore, the FDA imposed a requirement that REMS be required for all transmucosal fentanyl products. The class-wide REMS requirement includes education, healthcare provider and patient registration, and other elements to assure safe use. The FDA has the authority to remove from the market products that do not abide by the mandated REMS. In order for ONSOLIS® to be approved and launched, a REMS program needed to be accepted by the FDA and put in place prior to launch. In October 2009, ONSOLIS® was launched in the U.S. with an accompanying restrictive REMS program.

Despite the requirement that all transmucosal fentanyl products have an approved REMS, the FDA did not reach agreement with Teva on a REMS program for Fentora® or Actiq® until July 21, 2011, nearly two years after the approval of ONSOLIS®. Teva announced initiation of their REMS program in mid-October 2011. The absence of a REMS program for competing fentanyl products resulted in an un-level competitive environment and a highly unfavorable selling environment for ONSOLIS®.

The FDA eventually abandoned individual REMS programs through the creation of a consortium consisting of all manufacturers of transmucosal fentanyl products. The goal of the group was to develop one single REMS program covering all products in the class. On December 29, 2011, the FDA approved a REMS program covering all transmucosal fentanyl products. The program, which is referred to as the Transmucosal Immediate Release Fentanyl (TIRF) REMS Access Program, was designed to ensure informed risk-benefit decisions before initiating treatment with a transmucosal fentanyl product, and while patients are on treatment, to ensure appropriate use. The approved program covers all marketed transmucosal fentanyl products under a single program which is meant to enhance patient safety while limiting the potential administrative burden on prescribers and their patients. One common program ended the disparity in prescribing requirements for ONSOLIS® compared to similar products.

In 2014, the overall market for transmucosal fentanyl products for breakthrough pain according to Symphony Health, totaled $437 million in the U.S. The first approved product for the management of breakthrough cancer pain was Actiq® (oral transmucosal fentanyl citrate) which, according to Symphony Health, generated $12 million in sales in 2014. Total sales for generic versions of Actiq®, available from multiple manufacturers including Covidien, Teva and Actavis, totaled $56 million over the same period. Fentora® utilizes an effervescent tablet which is administered buccally. Fentora® was approved and launched in late 2006 and according to Symphony Health, generated $118 million in sales in 2014.

In December 2008, ProStrakan announced receipt of marketing authorization from the German regulatory authorities for their fentanyl sublingual tablet (under the brand name Abstral®; licensed from Orexo AB) which was subsequently launched in a number of countries. In January 2010, Abstral® was approved in the U.S. by the FDA, and Prostrakan launched Abstral® in the second quarter of 2011. In June 2012, Orexo announced that they would re-acquire the rights to Abstral® in the U.S. and subsequently licensed U.S. rights to Galena Biopharma. Galena relaunched Abstral® in 2014 and cumulative sales totaled $20 million at year end.

In the U.S., additional products have been approved by the FDA utilizing other delivery technologies to administer fentanyl. These products include intranasal Lazanda®, which was approved in June 2011, and a fentanyl sublingual spray formulation from Insys known as Subsys®, which received FDA approval in January 2012. Subsys®, which was launched in early 2012, was the first sublingual spray formulation of fentanyl, and the first product shown to relieve pain within five minutes. The rapid onset of action, coupled with aggressive promotion and a significant co-pay support program, has led to rapid growth. In 2014, Subsys® achieved a prescription market share in excess of 36%, or $217 million in sales.

Other potent pain products are also in development, including ARX-02 from AcelRx Pharmaceuticals, Inc. (NASDAQ:ACRX) which has a nano-tab drug/device delivery system containing sufentanil for the treatment of breakthrough pain. While we have limited information regarding this and potential other competitors and their development status and strategy, we believe that our technology may be differentiated because unlike these potential competitors, ONSOLIS® has a predefined residence time on the buccal membrane providing for consistent drug delivery from dose to dose. We believe that all of the competitive formulations of fentanyl will have

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intra-dose variability, meaning the patient may not get the same response each time the product is administered. In addition, it is our belief that the other competitive products may have tolerability issues and a higher level of potential abuse based on how they are delivered.

The chart below lists products or products in development that we believe may compete directly with ONSOLIS®.

Product	Company	Description	Status
Actiq® (oral transmucosal fentanyl citrate)	Teva/Generics	Fentanyl lozenge	Marketed (generics available)
Fentora® (fentanyl buccal tablet)	Teva	Effervescent buccal tablet	Marketed
Abstral® (fentanyl sublingual tablet)	Galena Biopharma	Sublingual tablet	Marketed
Lazanda® (fentanyl nasal spray)	DepoMed	Nasal spray	Marketed
Subsys® (fentanyl sublingual spray)	INSYS Therapeutics	Sublingual spray	Marketed
Fastanix/NAL 1239	NAL Pharmaceuticals	Orally dissolving film	Proposed ANDA
ARX-02	AcelRx Pharmaceuticals	Nanotab containing sufentanil	Phase 2 (U.S.)

In Europe, the total market for transmucosal fentanyl products continues to grow with the availability of new formulations, including ONSOLIS (marketed as BREAKYL in Europe by Meda). Multiple formulations of fentanyl have recently been approved and launched in Europe for the treatment of breakthrough cancer pain, including Abstral®, Effentora®, and Instanyl® (intranasal fentanyl spray).

BELBUCA (*BEMA® Buprenorphine) for chronic pain*

Chronic pain is often defined as any pain lasting more than 12 weeks. Whereas acute pain is a normal sensation that alerts us to possible injury, chronic pain persists often for months or even longer. Chronic pain may arise from an initial injury, such as back sprain, or there may be an ongoing cause, such as an illness. Sometimes there is no clear cause. According to the National Institutes of Health, approximately 100 million people in the U.S. are living with chronic pain.

BELBUCA is intended to meet the need for a new narcotic and would be used for chronic pain, including lower back, osteoarthritis and rheumatoid arthritis. Compared to currently marketed products and products under development, we believe that BELBUCA will be differentiated based on the following features:

- efficacy similar to morphine, but unlike morphine, is a Schedule III narcotic. Such regulatory designation indicates it is less prone to abuse and addiction and more convenient for physicians to prescribe (with prescription refills possible), pharmacists to dispense, and patients to obtain;

- broad applicability across a wide spectrum of patients with varying types of moderate to severe pain, and can be used as a sole-therapy or in combination with less potent analgesics such as non-steroidal anti-inflammatory drugs (NSAIDS);

longer half life which allows for less frequent dosing, thus potentially increasing patient compliance;

established safety profile (based on other dosage forms currently in the marketplace both in the U.S. and Europe) compared to agents in development; and

improved tolerability, including a lower incidence of constipation and, based on its Schedule III designation, a lower propensity for addiction and abuse versus other opioid analgesics.

The BEMA® delivery system may enable us to provide this opioid in a form suitable for ambulatory care and, because of the safety advantage associated with this opioid, we believe that BELBUCA could be an ideal next step product for patients with incomplete pain relief on non-narcotic analgesics.

The pain market is well established, with many pharmaceutical companies marketing innovative products as well as generic versions of older, non-patent protected products. In 2014, according to data from Symphony Health, the U.S. opioid market exceeded $10 billion in annual sales. Due to the ability of BELBUCA to potentially participate in the chronic pain market, we estimate that BELBUCA for chronic pain has the potential to exceed $500 million in annual peak sales. BELBUCA is currently under review by FDA for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options don t exist. A number of products may be competitors to BELBUCA . A potential focus will be to position BELBUCA as a step up from NSAIDs instead of, or prior to, the common practice of prescribing hydrocodone containing

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combinations or the more addictive Schedule II narcotics. Indications for such use include pain associated with lower back and severe arthritis conditions. Marketed competitors for these indications include Tramadol (Ultram® ER from PriCara and Ryzolt® from Purdue), hydrocodone containing combination and extended release (Zohydro®) formulations, Butrans® (buprenorphine transdermal patch from Purdue) and the potent opioids such as OxyContin® from Purdue, Avinza® from Pfizer, Kadian® from Actavis and Nucynta® ER from DepoMed and others. Other competition includes multiple generic opioid formulations, new chemical entities in clinical development with different mechanisms of action and various combination formulations. We also believe that other companies may be exploring the use of buprenorphine in other delivery technologies, though we believe such products lag significantly behind BELBUCA . This includes a sublingual spray formulation of buprenorphine from Insys which is being developed for the treatment of acute pain.

Additionally, abuse deterrent formulations of pain products are currently being marketed, in clinical development or under FDA review. These formulations, such as Embeda® and, Exalgo®, as well as new formulations of OxyContin® and Opana® ER use a variety of technologies to try and minimize abuse. New abuse deterrent formulations include Targiniq® ER (oxycodone/naloxone) and Hysingla ER (hydrocodone). Abuse deterrent products are likely to play an unclear but increasingly important role in prescribing, potentially even replacing the original product. An advantage of BELBUCA is that the compound, buprenorphine, may be inherently less likely to cause abuse and addiction given the lower propensity for the product to cause euphoria and is the current basis of its CIII classification.

The first buprenorphine formulation for the treatment of chronic pain was approved in 2010. Purdue Pharmaceuticals received FDA approval for Butrans® (buprenorphine transdermal system) in July. Butrans® is indicated for the management of moderate to severe chronic pain and delivers buprenorphine transdermally (through the skin) over a period of seven days. The approval of Butrans® signaled the interest and approvability of new formulations of buprenorphine. It is our view that the flexibility of dosing with a BEMA® formulation, wider range of doses and ease of use will make it a preferred formulation for a significant number of patients with chronic pain conditions. Butrans® was launched in early 2011. Sales of Butrans® in 2014 totaled over $192 million and continue to steadily grow. While limited information is available, other formulations of buprenorphine may also be in early stages of development for the treatment of pain.

In August 2014, the U.S. Drug Enforcement Administration (DEA) published in the Federal Register their final ruling moving hydrocodone combination products (such as Vicodin, Lortab, Norco, etc.) from Schedule III to the more-restrictive Schedule II, as recommended by the Assistant Secretary for Health of the U.S. Department of Health and Human Services (HHS) and as supported by the DEA s own evaluation of relevant data. As a result of the ruling, hydrocodone containing products are now classified in the same category (Schedule II) as morphine and oxycodone. As a result of the change to Schedule II, access to these products will be more restricted. Among other changes, written prescriptions will be required and refills will not be permitted. The ruling also conveyed findings that hydrocodone combination products have a higher risk of abuse and addiction compared to Schedule III products. The ruling went into full effect in October 2014.

We recognized early the value of buprenorphine in the treatment of pain. Buprenorphine is one of the few remaining Schedule III opioids and has a lower risk of abuse and addiction compared to Schedule II opioids and thus will have fewer restrictions on dispensing. BELBUCA has the opportunity to provide a Schedule III option for the treatment of chronic pain and thus helping to replace the void left from the hydrocodone combination products. We believe the actions taken to restrict the use of hydrocodone combination products may markedly increase the utility and appeal of BELBUCA as it now addresses an important unmet medical need for Schedule III options.

In addition to direct competitors, there are other factors that impact the market for pain products in general. The significant pricing pressures and availability of generic products in the U.S. and other regions are likely to have

increasing influence on the pharmaceutical market, including pain products. Additionally, opioids continue to garner increased scrutiny based on the growing problem of prescription drug abuse and addiction. It remains unclear what steps, if any beyond the reclassification of hydrocodone, the FDA or other government agencies may take to address the problem of opioid abuse and addiction. However, in July 2012 the FDA approved a class-wide REMS program for the extended release and long-acting opioids. The class-wide REMS program consists of a REMS-compliant educational program offered by an accredited provider of continuing medical education, patient counseling materials and a medication guide. BELBUCA is anticipated to fall within the existing class-wide REMS program.

BUNAVAIL®

In June 2014, BUNAVAIL® was approved by the FDA for the maintenance treatment of opioid dependence. BUNAVAIL® contains the partial opioid agonist buprenorphine, which binds to the same receptors as opiate drugs but has a higher affinity, slower onset and is both less addictive and less lethal in overdose. Naloxone, an opioid antagonist, is included as an abuse deterrent. When used as directed, the naloxone is swallowed and minimally absorbed; however, if misused (ie, dissolved and injected), the naloxone rapidly precipitates withdrawal symptoms.

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Maintenance treatment with buprenorphine reduces the typical cravings and withdrawal symptoms associated with coming off opioid prescription painkillers and heroin. This allows the individual suffering from an addiction to opioids along with counseling and support to work toward recovery. On average, treatment lasts a couple months, reflecting relatively high dropout rates, but a significant number of people remain on buprenorphine treatment chronically, with nearly one-quarter of patients still on therapy after nine months. BUNAVAIL® provides an alternative treatment utilizing the advanced BEMA drug delivery technology. BUNAVAIL® provides the highest bioavailability of any buprenorphine-containing product for opioid dependence, allowing for effective treatment with half the dose compared to Suboxone film. Additionally, BUNAVAIL® offers convenient and discrete buccal administration and avoids the need for patients to avoid talking and swallowing during administration. Data has also demonstrated an excellent tolerability profile with a 68% reduction in the incidence of constipation in a Phase 3 trial in patients converted from Suboxone® sublingual tablets or film to BUNAVAIL® at the end of 12 weeks.

The total market for buprenorphine containing products for opioid dependence approached $1.8 billion in 2014. The market has grown significantly as a result of the rapidly escalating problem of prescription opioid misuse and abuse, a recent resurgence of heroin use, the growing number of physicians treating opioid dependence, and the inclusion of addiction treatment as an essential benefit in the Affordable Care Act. We estimate that BUNAVAIL® for the maintenance treatment of opioid dependence has the potential to achieve from between $200 to $250 million in annual peak sales.

The products currently marketed for this indication include Suboxone®, a sublingual film formulation of buprenorphine and naloxone, a sublingual tablet, Zubsolv®, and generic formulations of both buprenorphine and buprenorphine/naloxone tablets. Suboxone® film, the market leader, achieved sales of nearly $1.2 billion in the U.S. in 2014. While maintaining its dominance as the market leader in the U.S., Suboxone® film experienced a decline in sales and share due to increased use of generics and the availability of newer formulation of buprenorphine/naloxone. In December 2014, Reckitt Benckiser Group PLC, the manufacturer of Suboxone® sublingual tablets and films, announced that they completed the spin-off of that company s pharmaceutical business (including the Suboxone® brand) under the name Indivior PLC in order to allow the consumer goods group to focus on its consumer health and hygiene products. The Indivior business will focus on addiction treatment and closely related areas including opioid overdose, cocaine overdose and alcohol dependence. In September 2012, Reckitt Benckiser announced that it had notified the FDA that they would be voluntarily discontinuing the distribution of Suboxone® tablets in the U.S. and subsequently halted further shipments in March 2013. The decision made by Reckitt Benckiser was reportedly due to accumulating data demonstrating significantly lower rates of accidental pediatric exposure with Suboxone® films compared with their tablet formulation due to the child-resistant, unit-dose packaging of the film versus a multi-dose bottle for the tablets. Additionally, Reckitt Benckiser filed a Citizens Petition to request that the FDA require all manufacturers of buprenorphine-containing products for the treatment of opioid dependence to implement public health safeguards including child-resistant, unit-dose packaging to reduce the risk of pediatric exposure. FDA subsequently rejected the Citizens Petition in February 2013, which allowed for the approval of the first generic formulations of Suboxone® tablets.

The actions taken by Reckitt Benckiser as well as patient preference for a film formulation of Suboxone® resulted in significant conversion of the Suboxone® market to the branded film formulation. In 2013, the sublingual film formulation of Suboxone® accounted for over 95% of total Suboxone® prescription sales.

Generic buprenorphine/naloxone tablet formulations were launched in early 2013 by Actavis and Amneal Pharmaceuticals and were followed by additional entrants including a generic formulation from Teva. The remaining prescription volume for Suboxone® tablets was rapidly converted to generics; however, the impact of generic buprenorphine/naloxone tablets on Suboxone® film sales has been somewhat limited to date. In 2014, generic buprenorphine/naloxone tablets accounted for 18% of total buprenorphine/naloxone sales. It is anticipated that

additional generics may enter the market, though the timing is unclear.

In terms of additional competition, Phase 3 trials were completed for Probuphine, a subcutaneous depot delivery system containing buprenorphine from Titan Pharmaceuticals (OTCBB:TTNP). Results of clinical studies demonstrated efficacy and safety, and Probuphine was submitted for FDA review in October 2012. Probuphine was anticipated to address the needs of the subset of patients undergoing treatment for opioid dependence who are unable to maintain compliance with alternative formulations or those who may be at high risk for diversion. In December 2012, Titan announced the signing of a license agreement with Braeburn Pharmaceuticals Sprl. The license grants Braeburn exclusive commercialization rights in the United States and Canada. In April 2013, the FDA issued a Complete Response Letter for Probuphine and requested additional data regarding its efficacy. An additional Phase 3 study assessing the efficacy and safety of Probuphine was initiated in April 2014. In November 2014, Titan announced completion of enrollment in their ongoing Phase 3 study of Probuphine and expects to complete the study by the middle of 2015, allowing for a resubmission of their NDA in late 2015. Given the need for surgical implantation and removal, Probuphine is not expected to be a significant competitive threat to BUNAVAIL®.

A sublingual tablet, referred to as Zubsolv® or OX219, was approved by FDA in July 2013 and subsequently launched in September 2013. Zubsolv® is a sublingual formulation of buprenorphine/naloxone using Orexo s proprietary sublingual drug delivery technology. Orexo is a specialty pharmaceutical company with headquarters in Sweden. Orexo is developing treatments using their proprietary sublingual drug delivery technology, which includes the marketed product Abstral® that delivers fentanyl for the treatment of breakthrough cancer pain. In July 2013 Orexo announced the establishment of a commercial partnership with Publicis Healthcare Solutions. In May 2014, Orexo announced a new partnership with InVentiv Health for Zubsolv in the U.S.

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The sales efforts for Zubsolv® are supported by a contract sales organization (Inventive Health) and the product is being marketed predominantly based on its claims of improved taste and faster dissolve time compared to Suboxone®. Sales for Zubsolv® in 2014 totaled approximately $52 million in the U.S and a prescription market share of just over 3%.

While limited information is available, other formulations of buprenorphine may also be in early stages of development for the treatment of opioid dependence, including an oral capsule (NTC-510) from Nanotherapeutics, Inc. Three Phase 1 studies have been completed to date (two Phase 1a single dose pharmacokinetic studies and one Phase 1b, multidose pharmacokinetic study). It has been demonstrated that NTC-510 administered orally achieves appropriate serum buprenorphine concentrations for analgesia and could potentially be dosed once daily. Also in development is a sublingual spray formulation of buprenorphine/naloxone from Insys which completed a Phase 1 study and buprenorphine hemiadipate (RBP-6300) from Indivior, an oral abuse-deterrent formulation of buprenorphine using Capsugel drug delivery technology.

While we anticipate that the market for buprenorphine/naloxone products for the treatment of opioid dependence will get increasingly more competitive, we believe a BEMA® formulation of buprenorphine/naloxone has significant appeal given its buccal administration, enhanced delivery of buprenorphine, convenience, and lack of taste issues. We also believe that the increased number of companies promoting the use of buprenorphine containing-products for opioid dependence has the potential to create greater awareness and help to further expand what is already a significant and growing market.

Clonidine Topical Gel

In March 2013, we announced that we had entered into a worldwide licensing agreement with privately held Arcion, where we will develop and commercialize Clonidine Topical Gel (formerly ARC4558) for the treatment of PDN and potentially other indications. The PDN market is highly under-served by existing products and there is a strong scientific rationale for developing a topical treatment for PDN that delivers analgesia in a way that avoids systemic side effects.

Evidence has shown that clonidine stimulates an inhibitory receptor in the skin associated with pain fibers. Arcion has developed a patented topical gel formulation of clonidine and has assessed its effectiveness in reducing pain in PDN in a double-blind, placebo-controlled, Phase 2 study where the primary study endpoint was the change in pain intensity over a 3 month treatment period in diabetic foot pain. A significant treatment difference was seen in the planned subset analysis of diabetic patients who had documented evidence of functioning pain receptors in the skin of the lower leg (p=0.01, n=63) thus, at a minimum, supporting the effectiveness of topical clonidine in diabetic patients with functioning pain receptors of the skin. In the overall population that included patients without functioning nerve receptors , there was a trend favoring Clonidine Topical Gel (p=0.07, n= 182), though the overall results did not reach statistical significance.

Nearly 26 million people in the U.S. have diabetes according to the American Diabetes Association. A substantial number of these people have neuropathy as manifest by impaired sensation and pain in the extremities, most commonly the feet. Patients with PDN often experience debilitating pain symptoms that affect day-to-day functioning and quality of life. How diabetes causes a length-dependent neuropathy is unknown. In the prior double-blind, randomized, controlled trial approximately 50% of the patients with PDN demonstrated functional nociceptors in the skin in the painful region as revealed by a response to topical capsaicin. Clonidine is thought to relieve pain by decreasing the abnormal excitability of these functional nociceptors. Currently available oral treatments are modestly effective in relieving symptoms and are limited by systemic side effects and drug interactions. There are no topical products approved for the treatment of this painful condition.

Along with antidepressants, antiepileptic drugs (AEDs) are often used as a first-line therapy for PDN. The most commonly prescribed AEDs for PDN are gabapentin and pregabalin (Lyrica). The choice between them is mostly influenced by physicians preference for the more-favorable dosing attributes (less-frequent daily dosing, faster titration) of pregabalin in balance with price and accessibility. AEDs are commonly associated with side effects including somnolence, dizziness, and weight gain. If first-line AED or antidepressant monotherapy fails to provide acceptable pain relief, physicians initiate combination therapy. If AED/antidepressant combination therapy is not effective, physicians typically add a dual-acting opioid such as tramadol. For more-severe pain, physicians may add or switch to tapentadol ER (Nucynta ER), which is the first and only dual-acting opioid analgesic to gain approval for PDN in the U.S. If pain persists with the addition of tramadol or tapentadol, physicians often switch to a more potent opioid analgesic (e.g., oxycodone) while maintaining AED and/or antidepressant therapy. Although some experts acknowledge that strong opioids can be quite effective for PDN, they generally reserve this drug class for refractory cases and/or those with high pain intensity. For some PDN patients, particularly those experiencing highly localized pain, physicians may prescribe the lidocaine 5% patch (Lidoderm). Pain specialists generally consider that lidocaine is particularly beneficial for localized pain, and many physicians prefer it to oral agents because it does not cause systemic side effects and is easy to administer. In many cases, the patch is used in combination with an oral first-line AED and/or antidepressant therapy.

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Oral medications that are approved for the treatment of PDN include anticonvulsants such as Lyrica (pregabalin), the antidepressant Cymbalta® (duloxetine) and the opioid Nucynta® ER (tapentadol ER), with sales for the treatment of neuropathic pain totaling over $3 billion in the U.S. according to Datamonitor. These treatments are modestly effective in relieving symptoms and their use can be limited by adverse effects and drug interactions. Additional oral formulations in development include an extended release formulation of pregabalin from Pfizer.

Acorda Therapeutics is developing a concentrated (20%) topical liquid formulation of capsaicin (NP-1998 [formerly NGX-1998]) for the treatment of neuropathic pain. The product was formerly in development by NeurogesX, which licensed all U.S. rights as well as those of its 8% capsaicin patch (Qutenxa) to Accorda in July 2013. Acorda is planning to launch a Phase 3 clinical trial of NP-1998 in painful HIV (human immunodeficiency virus) peripheral neuropathy as the first potential indication for NP-1998. The company is also exploring the potential for additional indications, including painful diabetic neuropathy. In 2011, NeurogesX completed a Phase 2 trial in post herpetic neuralgia and results from the trial confirmed efficacy and safety. Teva and Xenon Pharmaceuticals are developing TV-45070 (formerly XEN402), a subtype selective ion channel inhibitor. TV-45070 has potentially broad application in nociceptive pain, including inflammatory pain, and neuropathic pain indications. TV-45070 is partnered with Teva in a milestone, royalty and co-promotion partnership. Using a topical (ointment) formulation of TV-45070, Teva has initiated a 300-patient Phase 2b clinical trial in osteoarthritis, or OA, of the knee, and data are expected in the third quarter of 2015. Teva is also developing topical TV-45070 in neuropathic pain indications, and is currently planning a Phase 2b clinical trial in patients with postherpetic neuralgia.

Buprenorphine Depot Injection

Despite the availability of effective treatments, including BUNAVAIL® buccal film, challenges remain regarding patient adherence to long-term buprenorphine treatment, which is critical to successfully manage opioid dependence. This has led to interest in alternative delivery systems for buprenorphine. One such opportunity is the development of an injectable, long-acting, depot formulation. Microsphere-based, long acting, buprenorphine injectable depot has the ability to change the treatment paradigm in opioid dependence and pain management. Such a dosage form provides improved therapy compliance through continuous delivery of drug for up to 30 days. In 2014, we entered into an exclusive agreement with Evonik to develop and commercialize a proprietary, injectable microparticle formulation of buprenorphine potentially capable of providing 30 days of continuous therapy following a single subcutaneous injection. While we plan to pursue an indication for the maintenance treatment of opioid dependence, we have also secured the rights and plans to develop a product for the treatment of chronic pain in patients requiring continuous opioid therapy. As part of the agreement, we will have the right to license the product(s) following the attainment of Phase 1 ready formulations. At that point, Evonik could receive downstream payments for milestones related to regulatory filings and subsequent NDA approvals as well as product royalties. Evonik has the exclusive rights to develop the formulation and manufacture the product(s).

Additional long-acting depot formulations of buprenorphine are also in develop including one from Indivior, RBP-6000, which uses Atrigel technology and is currently in Phase 2 development and a product licensed by Braeburn Pharmaceuticals in November 2014 utilizing a technology licensed from Camurus. The product referred to as CAM2038 from Camurus is being developed as both a 1-week and 1-month subcutaneous injection.

Licenses, Intellectual Property and Proprietary Information

Our intellectual property strategy is intended to maximize protection of our proprietary technologies and know-how and to further expand targeted opportunities by extension of our patents, trademarks, license agreements and trade secrets portfolio. In addition, an element of our strategic focus provides for varying specific royalty or other payment obligations by our commercial partners as our applicable intellectual property portfolio changes or business activity

reaches certain thresholds.

However, patent positions of biotechnology and pharmaceutical organizations are considered to be uncertain and involve complex legal and technical issues. There is considerable uncertainty regarding the breadth of claims in patent cases which results in varied degrees of protection. While we believe that our intellectual property position is sound, it may be that our pending patent applications will not be granted or that our awarded claims may be too narrow to protect the products against competitors. It is also possible that our intellectual property positions will be challenged or that patents issued to others prior to our patent issuance may preclude us from commercializing our products. It is also possible that other parties could have or could obtain patent rights which may cover or block our products or otherwise dominate our patent position.

BEMA® Technology

The drug delivery technology space is congested, although we do not believe that our BEMA® products are in conflict with, dominated by, or infringing any external patents and we do not believe that we require licenses under external patents for our BEMA® based products in the United States, it is possible, however, that a court of law in the United States or elsewhere might determine

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otherwise. If a court were to determine that we were infringing other patents and that those patents were valid, we might be required to seek one or more licenses to commercialize our products or technologies. We may be unable to obtain such licenses from the patent holders. If we were unable to obtain a license, or if the terms of the license were onerous, there may be a material adverse effect upon our business plan to commercialize these products.

This potential exists in our present litigation with MonoSol. MonoSol claimed in a litigation initiated in late 2010 that our confidential and trade secret manufacturing process for ONSOLIS® infringes their patented manufacturing process for thin films. We do not believe that we have infringed these claims. Moreover, we believe that the original claims in MonoSol patents 588, 292 and 891 are invalid or overbroad, and, in connection with inter partes and ex parte reexamination proceedings we have brought before the USPTO, the USPTO has either rejected and cancelled all claims, amended the original claims to make them narrower, or issued narrower, new claims replacing the broader original claims for each of the 588, 292 and 891 patents respectively. We also believe that the manufacturing processes for our product candidates, including BEMA® Buprenorphine and BUNAVAIL® do not infringe MonoSol s patents, at least because they do not meet the limitations of the original, amended or new claims of MonoSol s patents. We maintain our manufacturing processes for our BEMA® products and product candidates as trade secrets. Based on our examination of these patents, we do not believe our manufacturing processes infringe MonoSol s patents. On March 7, 2012, the court granted our motion to stay the case pending outcome of the reexamination proceedings in the USPTO. On July 3, 2012, the USPTO issued an ex parte reexamination certificate on the 891 patent, in which all original claims were amended to make them narrower. On August 26, 2012, the USPTO issued an ex parte reexamination certificate on the 292 patent, in which all the original broader claims were replaced with narrower, new claims. As for the 588 patent, at the conclusion of the reexamination proceedings (and its appeals process), on April 17, 2014, the Patent Trial and Appeal Board (or PTAB) of the USPTO issued a Decision on Appeal affirming the Examiner s rejection (and confirming the invalidity) of all the claims of the 588 Patent. MonoSol did not request a rehearing by the May 17, 2014 due date for making such a request and did not further appeal the Decision to the Federal Court of Appeals by the June 17, 2014 due date for making such an appeal. Subsequently, on August 5, 2014, the USPTO issued a Certificate of Reexamination cancelling the 588 Patent claims.

On March 1, 2011, we were granted a patent extending the exclusivity of the BEMA® drug delivery technology in Canada to 2027. The Canadian Patent No. 2,658,585 provides additional patent protection for ONSOLIS® and BELBUCA . In April 2012, the USPTO granted US Patent No. 8,147,866 (issued from US Patent Application No. 13/184,306), which will extend the exclusivity of the BEMA® drug delivery technology for BELBUCA and BUNAVAIL® in the United States from 2020 to 2027. In April 2014, the USPTO granted US Patent No. 8,703,177 (issued from US Patent Application No. 13/590,094), which will extend the exclusivity of the BEMA® drug delivery technology for BUNAVAIL® in the United States to at least 2032.

We own various patents and patent applications relating to the BEMA® technology. US Patent No. 6,159,498 (expiration date October 2016), US Patent No. 7,579,019 (expiration date January 22, 2020), US Patent No. 8,147,866 (expiration date July 23, 2027), Canadian Patent No. 2,658,585 (expiration date July 2027) and EP 0 973 497 (expiration date October 2017) are of particular value to our business and technology platform relating to the BEMA® delivery technology. On February 16, 2010, we filed a complaint with the United States Federal District Court for the District of Columbia, requesting the USPTO be required to further extend the patent term for US 7,579,019 from 835 days to 1,191 days. In March 2011, we prevailed in this case, and the patent expiration date of US Patent No. 7,579,019 is now extended from January 31, 2019 to January 22, 2020.

On January 22, 2014, MonoSol filed a Petition for Inter Partes Review (or IPR) on US Patent No. 7,579,019 with the USPTO. In the Petition, MonoSol is requesting an inter partes review because it is asserting that the claims of US Patent No. 7,579,019 are alleged to be unpatentable over certain prior art references. The USPTO instituted the IPR on the 019 Patent. The IPR could invalidate or validate in whole or in part, this patent. Accordingly, we are defending our

US Patent No. 7,579,019 vigorously in the IPR proceedings.

With respect to trademarks, BDSI®, BEMA® and BUNAVAIL® are registered trademarks of BioDelivery Sciences International, Inc. ONSOLIS® and BREAKYL are trademarks owned by Meda Pharmaceuticals, Inc. PAINKYL is a trademark owned by TTY Biopharm.

Clonidine Gel Product

On March 26, 2013, we entered into the Arcion Agreement with Arcion pursuant to which Arcion agreed to grant to us an exclusive commercial world-wide license, with rights of sublicense, under certain patent and other intellectual property rights of Arcion to develop, manufacture, market, and sell gel products containing clonidine (or a derivative thereof), alone or in combination with other active ingredients, for topical administration for the treatment of painful diabetic neuropathy and other indications (the Clonidine Gel Products).

Per the Arcion Agreement, we have exclusive rights to various patents pertaining to the Clonidine Gel Products. US Patent No. 6,147,102 (expiration date October 26, 2019), US Patent No. 6,534,048 (expiration date October 26, 2019), US Patent No. 8,026,266 (expiration date September 30, 2029) and their corresponding patents in other countries (*e.g.*, Australia, Canada, Germany, *etc*.) are of particular value to our business and technology platform relating to the Clonidine Gel Products.

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Although we do not believe that our Clonidine Gel Products are in conflict with, dominated by, or infringing any external patents and we do not believe that we require licenses under external patents for Clonidine Gel Products, it is possible, however, that a court of law in the United States or elsewhere might determine otherwise. If a court were to determine that we were infringing other patents and that those patents were valid, we might be required to seek one or more licenses to commercialize our products or technologies. We may be unable to obtain such licenses from the patent holders. If we were unable to obtain a license, or if the terms of the license were onerous, there may be a material adverse effect upon our business plan to commercialize these products.

Buprenorphine Depot Injection Product

On October 27, 2014, we entered into a definitive Development and Exclusive License Option Agreement (which we refer to as the Evonik Development Agreement) with Evonik pursuant to which Evonik agreed to grant two exclusive options to acquire exclusive worldwide licenses, with rights of sublicense, to certain patents and other intellectual property rights of Evonik to develop and commercialize certain injectable, extended release products containing buprenorphine (which we refer to as Buprenorphine Depot Injection Products). If such options are exercised, such licenses would be memorialized in a definitive license agreement.

Although we do not believe that any Buprenorphine Depot Injection Products would be in conflict with, dominated by, or infringing any external patents and we do not believe that we require licenses under external patents for Buprenorphine Depot Injection Products, it is possible, however, that a court of law in the United States or elsewhere might determine otherwise. If a court were to determine that we were infringing other patents and that those patents were valid, we might be required to seek one or more licenses to commercialize our products or technologies. We may be unable to obtain such licenses from the patent holders. If we were unable to obtain a license, or if the terms of the license were onerous, there may be a material adverse effect upon our business plan to commercialize these products.

Manufacturing

We rely on third-party manufacturers, packagers, and analytical testing laboratories to produce commercial product and developmental products for research, product development, and clinical supplies. We are currently party to the following manufacturing arrangements for different companies:

BUNAVAIL®

Effective July 30, 2014, we entered a Supply Agreement with ARx for manufacturing, and effective March 6, 2014, we entered a Supply Agreement with Sharp for packaging for BUNAVAIL® commercial supplies, respectively. Both companies underwent successful FDA preapproval inspections and will be subject to annual quality audits. Both our contracts are also supported by a quality assurance agreement requiring our counterparties to adhere to product quality standards and cGMP manufacturing and packaging requirements.

ONSOLIS®

Effective October 17, 2005, we entered into an agreement with Aveva pursuant to supply ONSOLIS® for clinical trials and commercial sale. Under the terms of this agreement, Aveva is the sole supplier of ONSOLIS® for the United States and Canada. The current agreement expires on October 15, 2015. On October 9, 2014, Aveva sent us written notice of their intent not to renew our supply agreement. Therefore, our supply agreement with Aveva will expire on October 15, 2015. We will seek alternative manufacturing arrangements for ONSOLIS® in the U.S. in the event we are able to secure a new commercial partner for the product.

On March 12, 2012, we announced the postponement of the U.S. re-launch of ONSOLIS® following the initiation of the class-wide REMS with two appearance issues raised by FDA during an inspection of Aveva s manufacturing facility. Specifically, the FDA identified the formation of microscopic crystals and a fading of the color in the mucoadhesive layer during the 24-month shelf life of the product. ONSOLIS® has been subsequently reformulated with 12 months of available stability data on the reformulated product.

In February 2015, we re-acquired the rights to the ONSOLIS® NDA from Meda. With the resolution of the appearance issue and 12 months of stability on the reformulated product, we plan to submit a prior approval supplement for this formulation by the end of the first quarter of 2015 seeking its approval which expected by the end of the third quarter of 2015.

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BREAKYL

Effective December 15, 2006, we entered into a process development agreement and a commercial Supply Agreement on April 26, 2012, both with LTS. Under the terms of this supply agreement, LTS is the exclusive manufacturer of BEMA® Fentanyl for all countries with exception of the United States and Canada. LTS continues to manufacture BREAKYL for MEDA since it was first launched in the E.U. in September 2012.

BELBUCA (BEMA® Buprenorphine)

Effective January 5, 2012, we entered a license and development agreement with Endo for BELBUCA. Over the past two years, the technical operations and supply activities have been gradually transitioned from BDSI to Endo. As a result of the licensing and developmental agreement, all of the commercial supply agreements will be negotiated by and the responsibility of Endo.

Clonidine Topical Gel

Effective October 22, 2014, we entered into a master service agreement with Ei LLC for formulation, analytical and manufacturing services, clinical supplies, packaging and product release for the Clonidine Topical Gel. We have also made similar arrangements with Frontage and Tapemark for bulk manufacture for initial clinical trial supplies and individual dose units packaging, respectively.

Buprenorphine Depot Injection

Effective October 27, 2014, we entered into an exclusive agreement with Evonik to develop and commercialize a proprietary long acting, sustained release, biodegradable microparticle buprenorphine formulation capable of providing 30 days of continuous therapy following a subcutaneous injection. Through the agreement, we also secured the license to Evonik-owned intellectual property related to products for the maintenance treatment of opioid dependence and for the treatment of chronic pain.

Sales and Marketing

Following, and assuming, completion of clinical development and regulatory approval for each candidate product, we will pursue one of several approaches (or a combination thereof) for marketing and selling our products. These include licensing the products to appropriate partners so that they can market and distribute the products for us, co-promotions where we would share in the sales promotion, or use of our own recently established contract sales organization. We have already utilized this strategy with regard to our approved product, ONSOLIS®/ BREAKYL with our licensing agreements with Meda world-wide except Taiwan (TTY) and South Korea (Kunwha) and our worldwide license and development agreement with Endo for BELBUCA for chronic pain.

This strategy was further implemented in 2014 with the creation of our own exclusive contract sales force for the launch of BUNAVAIL®. This existing sales force now provides us with the means to sell BUNAVAIL® but also affords us the opportunity to consider selling other products in our own portfolio or those in-licensed. Using our own sales force provides us with significantly more control over commercialization efforts and makes us capable of selling our own products in specialty pharmaceutical markets while leaving with partners promotional responsibilities for the large primary care audiences.

For BUNAVAIL®, we completed our plans to self-commercialize the product in early 2014 and successfully launched our contract sales force in September.

ONSOLIS®/BREAKYL

European Union

In September 2006, we secured an exclusive licensing and supply agreement with Meda for the commercialization rights for BEMA® Fentanyl in the E.U., which is being marketed in Europe under the trade name BREAKYL . The agreement between Meda and us specifies that Meda is responsible for all post-approval clinical studies and label expansion trials. BREAKYL received marketing authorization from the European regulatory authorities in October 2010 and has been launched in over thirteen European countries including Germany, France and the U.K.

North America

In September 2007, we secured an exclusive licensing and supply agreement with Meda for the commercialization rights for ONSOLIS®, under which Meda was responsible for the sales, marketing and distribution of ONSOLIS® in the U.S., Canada and Mexico. The agreement specified that ONSOLIS® was to be detailed in the primary position for a specified duration among target prescribers

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ONSOLIS® was commercially launched in the United States in mid-October 2009 following approval by the FDA in July 2009. Under the Meda agreement, ONSOLIS® commercial efforts were supported by a therapeutic specialty sales force assembled by Meda to target oncologists and pain management specialists treating breakthrough cancer pain. A specialty sales force consisting of experienced and well trained sales representatives were put in place to promote ONSOLIS® to target healthcare providers.

ONSOLIS® was approved by the Canadian regulatory authorities in May 2010, and is the first product approved in Canada for the management of breakthrough cancer pain. Meda Valeant Pharma Canada Inc., a joint venture between Meda and Valeant Canada Limited is responsible for promotion of ONSOLIS® in Canada. ONSOLIS® was launched in Canada in the third quarter of 2011.

On March 12, 2012, we announced the postponement of the U.S. re-launch of ONSOLIS® following the initiation of the class-wide REMS until the product formulation could be modified to address two appearance-related issues. Such appearance-related issues involved the formation of microscopic crystals and a fading of the color in the mucoadhesive layer, raised by the FDA during an inspection of our North American manufacturing partner for ONSOLIS®, Aveva. While the appearance issues do not affect the product s underlying integrity, safety or performance, the FDA believes that the fading of the color in particular may potentially confuse patients, necessitating a modification of the product and its specification before it can be manufactured and distributed. The source of microcrystal formation and the potential for fading of ONSOLIS® was found to be specific to a buffer used in its formulation. We modified the formulation and as of the date of this report have 12 months of stability data on the reformulated product that shows no signs of microcrystal formation or color changes.

On January 27, 2015, we announced that we had entered into the Assignment Agreement with Meda to return to us the marketing authorizations for ONSOLIS® for the U.S. and the right to seek marketing authorizations for ONSOLIS® in Canada and Mexico, back to us. Once the NDA has been returned, we will have the right to work directly with the FDA and submit a prior approval supplement that responds to FDA questions and requests and will hopefully lead to the re-introduction of the product. FDA s review of the application may take up to six months; therefore, we could receive a decision before the end of 2015.

Additional Territories

On January 2, 2009, we entered into amendments to our agreements with Meda to grant Meda worldwide commercialization rights for ONSOLIS®/BREAKYL with the exception of Taiwan and South Korea. The sales royalties to be received by us will be the same for all territories as agreed to for Europe.

In 2010, licensing agreements were secured in Taiwan and South Korea providing the opportunity for commercialization in all territories globally. In May 2010, we announced a commercial partnership with Kunwha for the exclusive rights to develop and commercialize ONSOLIS® in the Republic of Korea. The agreement results in potential milestone payments of up to $1.275 million, which included the upfront payment of $0.3 million and royalties based on net sales. In October 2010, a commercial partnership with TTY was announced, providing commercialization rights for Taiwan. This agreement results in potential milestone payments of up to $1.3 million along with royalties based on sales and included an upfront payment of $0.3 million.

In November 2011, we announced that TTY had submitted a NDA for marketing authorization of BEMA® Fentanyl to the Taiwan Food and Drug Administration. This triggered a milestone payment to us of approximately $0.3 million, which was received November 2011. In July 2013, we announced the regulatory approval of BEMA® Fentanyl in Taiwan, where the product will be marketed under the brand name PAINKYL . The approval in Taiwan resulted in a milestone payment of $0.3 million to us, which was received in the third quarter 2013.

We believe that utilizing commercial partners to market and sell ONSOLIS®/BREAKYL relieves us of the burden associated with a significant increase in expenditures or headcount otherwise associated with a commercial launch of a first product. Additionally, we believe our commercial partnerships for ONSOLIS®/BREAKYL allows internal efforts to be focused on the development of our pipeline of products.

BELBUCA (BEMA® Buprenorphine) for Chronic Pain

We announced the signing of a world-wide licensing and development agreement for BELBUCA with Endo in January 2012. Under terms of the agreement, Endo will be responsible for the manufacturing, distribution, marketing and sales of BELBUCA on a worldwide basis.

Endo is one of the premier companies in the area of pain management and has demonstrated significant success in the pain space particularly with the development, launch and commercialization of a portfolio of pain therapeutics including Opana® ER,

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Lidoderm® and Voltaren® Gel. Endo s long experience in pain includes a strong sales and marketing capability, with sales representatives that are established in the offices of many high value healthcare practitioners who are high prescribers of opioids and other pain products.

We believe that BELBUCA is an excellent fit to Endo s pain portfolio and will, if approved by the FDA, provide Endo with an additional pain product that can be aligned with other products in their portfolio based on factors such as pain severity and opioid scheduling. Endo will be responsible for all sales and marketing at the time of launch and will focus their promotional and educational efforts on high volume prescribers of opioids and other analgesics, which includes predominantly pain management specialists and primary care physicians. Endo will commercialize BELBUCA outside the U.S. through its own efforts or through regional partnerships. We believe that BELBUCA would potentially be aligned with the needs of pain specialists and primary care physicians who seek an alternative to Schedule II opioids for the treatment of moderate to severe chronic pain that is not adequately controlled with commonly prescribed first-line therapies (e.g. NSAIDs).

BUNAVAIL®

During 2013, we engaged in the process of assessing a variety of strategic options for the commercialization of BUNAVAIL® in the U.S. The options we explored included commercial partnerships, co-promotion arrangements, leading commercial efforts internally through the use of contract resources, or a combination of the aforementioned strategic options. Outside the U.S., we will likely pursue partnerships.

Following a thorough assessment of commercialization options for BUNAVAIL®, we identified BUNAVAIL® as an attractive product to build a commercial presence capable of supporting both BUNAVAIL® and our other future products. Additionally, the self-commercialization of BUNAVAIL® supports our longer term vision to become a fully integrated pharmaceutical company. The dynamics of the opioid dependence market made self-commercialization a feasible and attractive option. In total, approximately 90% of all prescriptions are written by approximately 5,000 physicians which include primary care physicians, psychiatrists, addiction medicine specialists and pain specialists, with most concentrated in the eastern third of the U.S. and the west coast, allowing for coverage of a majority of the prescriber base with a modest sized sales force. Sales force sizing estimates suggest that a field sales force of approximately 60 could reach most of the identified target audience with the necessary frequency. Additionally, the relatively small prescriber base along with the limited number of competitors results in relatively modest marketing expenditures. And finally, the high awareness and physician acceptance of buprenorphine for the treatment of opioid dependence lessens the need for costly educational and promotional programs.

Plans to self-commercialize BUNAVAIL® were completed in early 2014. We chose to utilize internal resources to provide the strategic direction and oversight of specialized contractor resources. In March 2014, we entered into an agreement with Quintiles to support the launch of BUNAVAIL®. Under terms of the agreement, Quintiles provides a range of services to support the commercialization of BUNAVAIL® in the U.S., including recruiting and training a field sales force. Separately, we entered into an agreement with Ashfield Market Access to provide managed markets and trade support for BUNAVAIL®. Ashfield Market Access, which is led by industry veterans including those who led GlaxoSmithKline s managed markets group for more than 20 years, took responsibility for executing a payer strategy aimed at maximizing patient access to BUNAVAIL®.

We began our efforts at the 2014 annual meeting of the American Society of Addiction Medicine (ASAM) with deployment of a contract Medical Science Liaison (MSL) team under the oversight of Medical Affairs. Following ASAM, the MSL team focused on introducing physicians to the BEMA® technology.

Under full oversight of BDSI, recruitment and hiring of our specialty addiction sales force was completed during the third quarter of 2014. A highly experienced sales force with significant experience in the areas of pain and addiction medicine was deployed. Approximately 60% of representatives hold ten or more years of pharmaceutical sales experience and nearly 90% with five or more years of experience. Three-quarters of the field force previously had prior experience in the areas of pain management or addiction medicine.

On November 3, 2014, we announced the availability of BUNAVAIL® in the U.S. where it is being supported by a 60-person field sales force and a full marketing effort targeting the nearly 5,000 physicians who are responsible for approximately ninety percent of prescriptions for buprenorphine products for the treatment of opioid dependence. The launch was also supported by a full marketing effort aimed at increasing product awareness including advertising and promotion, direct mail and email, a speakers programs and a number of initiatives, including a copay support program, to minimize access issues.

We recognize the competitive nature of the opioid dependence market and will continuously evaluate the size and structure of our sales force relative to our competitors. As appropriate for our business, we will consider the deployment of additional sales territories and representatives. While we recognize that we may not be able to support a sales force the size of an established competitor such as Indivior (formerly Reckitt Benckiser), we believe we can maintain a competitive share of voice through both personal and non-personal selling efforts. We also believe that BUNAVAIL® offers distinct and important benefits over other products in the opioid dependence market which will allow it to successfully compete in the long term.

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Government Regulation

The nonclinical and clinical development, manufacturing and marketing of any drug product, is subject to significant regulation by governmental authorities in the United States and other countries. Complying with these regulations involves considerable time, expense and uncertainty.

In the United States, drugs are subject to rigorous federal regulation and, to a lesser extent, state regulation. The Federal Food, Drug and Cosmetic Act, as amended, and the regulations promulgated thereunder, and other federal and state statutes and regulations govern, among other things, the testing, manufacture, safety, efficacy, labeling, storage, record keeping, approval, advertising and promotion of our drugs. Drug development and approval within this regulatory framework is difficult to predict, requires a number of years and involves the expenditure of substantial resources. Moreover, ongoing legislation by Congress and rule making by the FDA presents an ever-changing landscape where we could be required to undertake additional activities before any governmental approval to market our products is granted.

The steps required before a pharmaceutical product may be marketed in the United States include:

1. small scale manufacturing of the product;

2. laboratory and nonclinical tests for safety of the product;

3. submission of an IND to the FDA for the product which must become effective before human clinical trials can commence;

4. larger scale manufacturing of the product;

5. clinical trials to characterize the efficacy and safety of the product in the intended patient population;

6. submission of an NDA to the FDA; and

7. approval of the NDA by the FDA.

In addition to obtaining FDA approval for each product, each product-manufacturing establishment must be registered with, and approved by, the FDA. Manufacturing establishments are subject to biennial inspections by the FDA and must comply with the FDA s Good Manufacturing Practices and with other federal and local regulations.

Nonclinical Trials

Nonclinical testing includes laboratory evaluations of the active drug substance and formulation, as well as tissue culture and animal studies to assess the safety and potential efficacy of the investigational product. Nonclinical tests must be conducted by laboratories that comply with FDA Good Laboratory Practices regulations. Nonclinical testing

is inherently risky and the results can be unpredictable or difficult to interpret. The results of nonclinical testing are submitted to the FDA as part of an IND and are reviewed by the FDA prior to the commencement of clinical trials. Unless the FDA places a clinical hold on an IND, clinical studies may begin thirty (30) days after the IND is submitted.

We have relied and intend to continue to rely on third party contractors to perform nonclinical trials.

Clinical Trials

Clinical trials involve administration of the investigational product to healthy volunteers and/or to patients under the supervision of a qualified investigator. Clinical trials must be conducted in accordance with Good Clinical Practices following protocols acceptable to FDA that detail the objectives of the study, the parameters to be used to monitor safety and the efficacy and the planned evaluation of results. Each protocol must be submitted to the FDA prior to its conduct. Further, each clinical study must be conducted under the auspices of an independent institutional review board that protects the rights and welfare of the study subjects. The drug product used in clinical trials must be manufactured according to Good Manufacturing Practices.

Clinical trials are typically conducted in three sequential phases, but the phases may overlap and not all phases may be necessary when developing investigational products that will utilize the FDA s 505(b)(2) approval process. Phase 1 studies are typically performed in normal healthy volunteers to assess the safety (adverse side effects), absorption, metabolism, bio-distribution, excretion, and food and drug interactions of the investigational drug product. Additional studies may be performed to assess abuse potential as well as limited measures of pharmacologic effect. Phase 2 is the proof of principle stage and involves studies in a limited number of patients in order to:

assess the potential efficacy of the product for specific, targeted indications;

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identify the range of doses and dose regimens likely to be effective for the indication; and

identify possible adverse events and safety risks.

When there is evidence that the product may be effective and has an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to establish the clinical efficacy and safety profile of the product within a larger population at geographically dispersed clinical study sites. Phase 3 frequently involves randomized controlled trials and, whenever possible, studies are conducted in a manner so that neither the patient nor the investigator knows what treatment is being administered. We, or the FDA, may suspend clinical trials at any time if it is believed that the individuals participating in such trials are being exposed to unacceptable health risks.

We have in the past and will continue to rely upon third party contractors to advise and assist us in the preparation of our INDs and the conduct of clinical trials that will be conducted under the INDs.

New Drug Application and FDA Approval Process

The results of the pharmaceutical and manufacturing development work, nonclinical studies and clinical studies are submitted to the FDA in the form of an NDA for approval to market and sell the product. The testing and approval process is likely to require substantial time and effort. In addition to the results of nonclinical and clinical testing, the NDA applicant must submit detailed information about chemistry, manufacturing and controls that will describe how the product is made, packaged, labeled, and tested through the manufacturing process. The manufacturing process continues to develop throughout the period of clinical trials such that at the time of the NDA, it has been demonstrated that there is control of the process and the product can be made consistently at commercial scale.

The NDA review process involves FDA investigation into the details of the manufacturing process, as well as the design and analysis of each of the nonclinical and clinical studies. This review includes inspection of the manufacturing facility, the data recording process for the clinical studies, the record keeping at a sample of clinical trial sites and a thorough review of the results for each nonclinical and clinical study. Through this review, the FDA reaches a decision about the risk-benefit profile of a product candidate. If the benefit outweighs the risk, the FDA begins negotiation with the company on the content of an acceptable package insert and an associated REMS plan if required.

The NDA review process is affected by a number of factors, including the severity of the disease, the availability of alternative treatments, and the risks and benefits demonstrated in clinical trials. Consequently, there is a risk that approval may not be granted on a timely basis, if at all. The FDA may deny approval of an NDA if applicable regulatory criteria are not satisfied. Moreover, if regulatory approval of a product is granted, such approval may entail limitations on the indicated uses for which it may be marketed, require additional testing or information, or require post-marketing testing (Phase 4) and surveillance to monitor the safety of a company s product if it does not believe the NDA contains adequate evidence of its safety. Finally, product approvals may be withdrawn if compliance with regulatory standards is not maintained or health problems are identified that would alter the risk-benefit analysis for the product. Post-approval studies may be conducted to explore the use of the product for new indications or populations such as pediatrics.

Among the conditions for NDA approval is the requirement that any prospective manufacturer s quality control and manufacturing procedures conform to Good Manufacturing Practices and the specifications approved in the NDA. In complying with standards set forth in these regulations, manufacturers must continue to expend time, money and effort in the area of quality control and quality assurance to ensure full technical compliance. Manufacturing establishments, both foreign and domestic, also are subject to inspections by or under the authority of the FDA and by

other federal, state or local agencies. Additionally, in the event of non-compliance, the FDA may issue warning letters and/or seek criminal and civil penalties, enjoin manufacture, seize product or revoke approval.

Risk Evaluation and Mitigation Strategy

In March 2008, new legislation designated as the Food and Drug Administration Amendments Act of 2007 (the FDAAA) took effect. This legislation strengthened the FDA s authority over drug safety and directs the FDA to develop systems aimed at managing the risk-benefit ratio of a drug, with a particular focus on post-approval safety. FDAAA authorized the FDA to require and enforce a Risk Evaluation and Mitigation Strategy, or REMS, if the FDA determines that it is necessary to ensure that the benefits of a drug outweigh the potential risks. The legislation also provides the FDA with increased authority to require REMS at any point in a drug product s lifecycle based on new safety information.

A REMS is defined by the FDA as a strategy to manage a known or potential serious risk associated with a drug or biological product. The FDA s assessment of whether to require a REMS as a condition for approval considers factors such as the size of the population likely to use the drug, the seriousness of the disease or condition that is to be treated by the drug, the expected benefit, and the seriousness of any known or potential adverse events that may be related to the drug. A REMS may be conveyed through the use of a number of tools including a Medication Guide for distribution when the drug is dispensed, a communication plan to physicians to convey potential risks, and elements to ensure safe use. These elements may include provisions that healthcare providers who prescribe the drug and pharmacists who dispense the drug have particular training, experience or special certifications; that the drug be

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dispensed only in certain healthcare settings; that the drug be dispensed to patients with evidence of safe-use conditions; and/or that patients must be enrolled in a registry. Under the FDAAA, the FDA has also been granted enforcement authority over violations of the REMS provisions. The FDA may impose civil monetary penalties, the drug or biological product can be deemed misbranded, and/or the FDA may obtain injunctive relief against further distribution of the product.

On December 29, 2011, the FDA approved a class-wide REMS program covering all transmucosal fentanyl products under a single risk management program. ONSOLIS® is subject to this REMS.

Additionally, FDA has implemented a class-wide REMS covering the extended release and long acting opioid class. The class-wide REMS program consists of a REMS-compliant educational program offered by an accredited provider of continuing medical education, patient counseling materials and a medication guide. BELBUCA is anticipated to fall within the existing class-wide REMS program. The cost and implementation of the extended release and long-acting opioid REMS is shared among multiple companies in the category.

There also continues to be a REMS in place for buprenorphine for the treatment of opioid dependence. BUNAVAIL® is included in this existing REMS that is far less cumbersome than the ONSOLIS® REMS and includes a medication guide and healthcare professional and patient education.

International Approval

Whether or not FDA approval has been obtained, approval of a product by regulatory authorities in foreign countries must be obtained prior to the commencement of commercial sales of the drug in such countries. The requirements governing the conduct of clinical trials and drug approvals vary widely from country to country, and the time required for approval may be longer or shorter than that required for FDA approval. Although there are some procedures for unified filings for certain European countries, in general, each country at this time has its own procedures and requirements.

Other Regulation

In addition to regulations enforced by the FDA, we are also subject to United States regulation under the Controlled Substances Act, the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act and other present and potential future federal, state, local or similar foreign regulations. Our research and development may involve the controlled use of hazardous materials, chemicals and radioactive compounds. Although we believe that our safety procedures for handling and disposing of such materials comply with the standards prescribed by state and federal regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of any accident, we could be held liable for any damages that result and any such liability could exceed our resources.

Employees

As of March 12, 2015, we have 29 full-time employees. Thirteen are involved in our clinical development program and operations, eleven handle our administration, accounting and legal and five handle our internal sales and marketing. Advanced degrees and certifications of our staff include three Ph.Ds, two Pharm.Ds, one M.D., three CPAs, six MBAs, two MSs and one JD. None of our employees are covered by collective bargaining agreements. From time to time, we also employ independent contractors to support our engineering and administrative functions. We consider relations with all of our employees to be good. Each of our employees has entered into confidentiality, intellectual property assignment and non-competition agreements with us.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended (which we refer to herein as the Exchange Act), are filed with the SEC. Such reports and other information that we file with the SEC are available free of charge on our website at http://bdsi.investorroom.com/sec_filings when such reports are available on the SEC website. The public may read and copy any materials that we file with the SEC at the SEC s Public Reference Room at 100 F Street, NE, Room 1580, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC at http://www.sec.gov. The contents of these websites are not incorporated into this filing. Further, the foregoing references to the URLs for these websites are intended to be inactive textual references only.

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Item 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. Before purchasing our common stock, you should carefully consider the following risk factors as well as all other information contained in this Report, including our consolidated financial statements and the related notes. The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties that we are unaware of, or that we currently deem immaterial, also may become important factors that affect us. If any of the following risks occur, our business, financial condition or results of operations could be materially and adversely affected. In that case, the trading price of our common stock could decline, and you may lose some or all of your investment.

Risks Relating to Our Business

We have incurred significant losses since inception, have relatively limited working capital and have only generated minimal revenues from actual products sales. As such, you cannot rely upon our historical operating performance to make an investment decision regarding our company.

From our inception in January 1997 and through December 31, 2014, we have recorded significant losses. Our accumulated deficit at December 31, 2014 was approximately $205.5 million. As of December 31, 2014, we had working capital of approximately $49 million, but we do not generate meaningful recurring revenue or cash flow and thus use our working capital to maintain our operations. Our ability to generate revenue and achieve profitability depends upon our ability, alone or with others, to complete the development of our product candidates and product concepts, obtain the required regulatory approvals and manufacture, market and sell our products if approved. We may be unable to achieve any or all of these goals.

Although we have generated licensing-related and other revenue to date, we have only recently begun to generate revenue from the commercial sales of our approved products ONSOLIS® and BUNAVAIL® and such revenue has been minimal to date. In the case of ONSOLIS®, sales have been adversely affected by: (i) the lack of a uniform REMS program at the time of the launch of ONSOLIS®, and (ii) certain post-FDA approval appearance issues associated with ONSOLIS® which have led to the temporary suspension of manufacturing and marketing of ONSOLIS® in the US and Canada. In the case of BUNAVAIL®, sales have been minimal as we have only recently commenced the commercial launch of the product and are subject to the risks of launching a new product. There is a risk that we will be unable to generate sustained and predictable revenues from product sales.

Since our inception, we have engaged primarily in research and development, licensing technology, seeking grants, raising capital and recruiting scientific and management personnel. Since 2005, we have also focused on clinical and commercialization activities, originally relating to ONSOLIS® and more recently with BELBUCA , BUNAVAIL® and Clonidine Topical Gel. This relatively limited operating history may not be adequate to enable you to fully assess our ability to develop and commercialize our technologies and proposed formulations or products, obtain FDA approval and achieve market acceptance of our proposed formulations or products and respond to competition. We may be unable to fully develop, obtain regulatory approval for, commercialize, manufacture, market, sell and derive material revenues from our product candidates or product concepts in the timeframes we project, if at all, and our inability to do so would materially and adversely impact our viability as a company.

There are risks associated with the recent launch of our BUNAVAIL® product. We thus cannot accurately predict the volume or timing of any future sales of our recently launched BUNAVAIL® product, making the timing of any revenues therefrom difficult to predict.

In 2014, we commenced the commercial launch of BUNAVAIL®, which represented the commencement of the first self-commercialization effort for our company. As such, our ability to establish and increase sales of BUNAVAIL® is

important to us, both for the revenue it may generate as well as to demonstrate our capabilities as an integrated specialty pharmaceutical company as opposed to a research and development organization. The commercial launch of any product is subject to significant risks, and particularly so for us given the size and relative experience of our company with commercial operations. In addition, we may be faced with lengthy customer evaluation and formulary and managed care approval processes associated with the launch of BUNAVAIL®. Consequently, we may incur substantial expenses and devote significant management effort and expense in developing customer trial and adoption of BUNAVAIL® which may or have an adverse impact on our ability to generate revenue from sales of this product. We must obtain as approval for commercial insurance and government reimbursement in order to initiate high volume sales of BUNAVAIL®, which approval is subject to risk, potential delays and contract terms, and which may not actually occur or may occur with less favorable terms. The sales of BUNAVAIL are also dependent on the effectiveness of our selling and promotional efforts as well as influenced by competitive activity, new product approvals, pricing pressure and generic entrants. As such, we cannot accurately predict the volume or timing of any future sales of BUNAVAIL®, and our inability to commercialize this product would likely have an adverse effect on our results of operations and public stock price.

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We have limited experience as a company in self-commercializing pharmaceutical products, which heightens the risks related to our self-commercialization of BUNAVAIL®.

To date, we have partnered our products with larger pharmaceutical companies, who have taken primary responsibility for development and commercialization activities for such products. We are presently self-commercializing BUNAVAIL®. As a company, prior to our commercialization of BUNAVAIL®, we had never been primarily responsible for manufacturing, supply chain, sales and marketing efforts for one of our products, and therefore our efforts with BUNAVAIL® are our initial efforts in this regard. Given this lack of experience, there is a risk that we may be unable to adequately execute, either on our own or through third parties, one or more elements of our commercial plans for BUNAVAIL®. If this were to occur, we may not achieve anticipated revenues from BUNAVAIL®, which would have a material adverse effect on our results of operations, cash flow, reputation and stock price.

If our competitors are successful in obtaining approval for Abbreviated New Drug Applications for products that have the same active ingredients as our BUNAVAIL® product, sales of our BUNAVAIL® product may be adversely affected.

Our competitors may submit for approval certain Abbreviated New Drug Applications (or ANDAs) which provide for the marketing of a drug product that has the same active ingredients in the same strengths and dosage form as a drug product already listed with the FDA, and which has been shown to be bioequivalent to such FDA-listed drug. Drugs approved in this way are commonly referred to as generic versions of a listed drug, and can often be substituted by pharmacists under prescriptions written for an original listed drug. Any applicant filing an ANDA is required to certify to the FDA that the new product subject to the ANDA will not infringe an already approved product s listed patents or that such patents are invalid (otherwise known as a Paragraph IV Certification).

A number of our competitor companies have filed Paragraph IV Certifications challenging the patent for Suboxone® film, the market leader in the field in which we expect to generate sales of BUNAVAIL®. To the extent that any company is successful in challenging the validity of certain patents covering Suboxone® film under a Paragraph IV Certification, it could result in FDA approval of a drug that is lower in price to Suboxone® film. Such a new drug could make it more difficult for BUNAVAIL® to gain any significant market share in an increasingly generic marketplace, which would have a material adverse effect on our results of operations, cash flow, reputation and stock price.

Until we are able to generate recurring and predictable revenues for commercial operations, we will likely need to raise additional capital from time to time to continue our operations or expand our business, and our failure to do so would significantly impair our ability to fund our operations, develop our technologies and product candidates, attract commercial partners, retain key personnel or promote our products.

Our operations have been funded almost entirely by external financing and not from commercial revenues. Such financing has historically come primarily from license and royalty fees, the sale of common and preferred stock and convertible debt to third parties, related party loans and, to a lesser degree, from grants and bank loans. At December 31, 2014, we had cash of approximately $70.5 million. Depending on BUNAVAIL® sales and receiving the Endo milestone payment, we may not need to raise capital to fund our foreseeable business activities. However, even without the Endo milestone and any business adjustments, we have sufficient cash into early 2016, although this assumes that we do not accelerate the development of other opportunities available to us, engage in an extraordinary transaction or otherwise face unexpected events, costs or contingencies, any of which could affect our cash requirements.

Depending on the timing and receipt of milestone payments from our commercial partnership with Endo and given our anticipated cash usage and lack of significant revenues, there is a risk that we will need to raise additional capital in the future to fund our anticipated operating expenses and progress our business plans. This will include in large part the need to fund the launch of BUNAVAIL and our current and potential new development activities. As a result, we may require significant additional capital to further our planned activities. If additional financing is not available when required or is not available on acceptable terms, we may be unable to fund our operations and planned growth, develop or enhance our technologies, take advantage of business opportunities or respond to competitive market pressures. Any negative impact on our operations may make raising additional capital more difficult or impossible and may also result in a lower price for our shares.

We may have difficulty raising any needed additional capital.

We may have difficulty raising needed capital in the future as a result of, among other factors, our lack of material revenues from sales, as well as the inherent business risks associated with our company and present and future market conditions. Our business currently only generates a small amount of revenue from product sales, and such current sources of revenue will likely not be

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sufficient to meet our present and future capital requirements. Therefore, given that we plan to continue to expend substantial funds on commercialization activities (including those relating to BUNAVAIL®) as well as potentially on other strategic initiatives, there is a risk that we will require additional capital to fund these activities. If adequate funds are unavailable, we may be required to delay, reduce the scope of or eliminate one or more of our research, development or commercialization programs, product launches or marketing efforts, any of which may materially harm our business, financial condition and results of operations.

Our long term capital requirements are subject to numerous risks.

Our long term capital requirements are expected to depend on many factors, including, among others:

- the number of potential products we have in development;
- progress and cost of our research and development programs;
- progress with non-clinical studies and clinical trials;
- time and costs involved in obtaining regulatory (including FDA) clearance and addressing regulatory and other issues that may arise post-approval (such as we have experienced with ONSOLIS®);
- costs involved in preparing, filing, prosecuting, maintaining and enforcing patent, trademark and other intellectual property claims;
- costs of developing sales, marketing and distribution channels and our ability to sell our products;
- costs involved in establishing manufacturing capabilities for commercial quantities of our products;
- costs we may incur in acquiring new technologies or products;
- competing technological and market developments;
- market acceptance of our products;
- costs for recruiting and retaining employees and consultants;

costs for training physicians; and

legal, accounting, insurance and other professional and business related costs.

We may consume available resources more rapidly than currently anticipated, resulting in the need for additional funding sooner than anticipated. We may seek to raise any necessary additional funds through equity or debt financings, collaborative arrangements with corporate partners or other sources, which may have a material effect on our current or future business prospects.

Our additional financing requirements could result in dilution to existing stockholders.

The additional financings which we have undertaken and which we will likely in the future require, have and may be obtained through one or more transactions that have diluted or will dilute (either economically or in percentage terms) the ownership interests of our stockholders. Further, we may not be able to secure such additional financing on terms acceptable to us, if at all. We have the authority to issue additional shares of common stock and preferred stock, as well as additional classes or series of ownership interests or debt obligations which may be convertible into any one or more classes or series of ownership interests. We are authorized to issue 75 million shares of common stock and 5 million shares of preferred stock. Such securities may be issued without the approval or other consent of our stockholders.

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Our Credit Agreement with MidCap Financial SBIC, LP (or MidCap) contains restrictions that limit our flexibility in operating our business. We may be required to make a prepayment or repay the outstanding indebtedness earlier than we expect under our Credit Agreement if a prepayment event or an event of default occurs, including a material adverse change with respect to us, which could have a materially adverse effect on our business.

In July 2013, we entered into a Credit Agreement with MidCap whereby we received a loan in the aggregate amount of $20 million. The agreement contains various covenants that limit our ability to engage in specified types of transactions. These covenants limit our ability to, among other things:

- incur or assume certain debt;
- merge or consolidate or acquire all or substantially all of the capital stock or property of another entity;
- change the nature of our business;
- change our organizational structure or type;
- amend, modify or waive any of our organizational documents;
- license, transfer or dispose of certain assets;
- grant certain types of liens on our assets;
- make certain investments;
- pay cash dividends;
- enter into material transactions with affiliates; and
- amend or waive provisions of material agreements in certain manners.

The restrictive covenants of the Credit Agreement could cause us to be unable to pursue business opportunities that we or our stockholders may consider beneficial. A breach of any of these covenants could result in an event of default under the Credit Agreement. An event of default will also occur if, among other things, a material adverse change in our business, operations or condition occurs, or a material impairment of the prospect of our repayment of any portion of the amounts we owe under the Credit Agreement occurs. In the case of a continuing event of default under the agreement, MidCap could elect to declare all amounts outstanding to be immediately due and payable and terminate

all commitments to extend further credit, proceed against the collateral in which we granted MidCap a security interest under the Credit Agreement, or otherwise exercise the rights of a secured creditor. Amounts outstanding under the Credit Agreement are secured by all of our existing and future assets (excluding certain intellectual property).

We may not have enough available cash or be able to raise additional funds on satisfactory terms, if at all, through equity or debt financings to make any required prepayment or repay such indebtedness at the time any such prepayment event or event of default occurs. In such an event, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant to others rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our business, financial condition and results of operations could be materially adversely affected as a result.

Until we enter into a replacement license agreement for the marketing of ONSOLIS® in North America, we will not receive revenues from our ONSOLIS® product.

In January of 2015, we entered into a definitive assignment agreement under which Meda transferred back to us the rights to marketing authorizations in the United States for ONSOLIS®**.** As a result, we must find a new strategic partner with whom we intend to enter into a potential replacement license. There is no assurance that we will find a replacement licensee for the ONSOLIS® marketing authorizations in a timely manner, or at all. If we fail to find a replacement licensee, we will not receive any royalty from revenues associated with the sale of ONSOLIS®, as contemplated by the original Meda license. In addition, we may be required to market the product without any assistance from a third party that specializes in the marketing within the product category and may be better equipped to effect a higher volume of sales. We may expend significant resources to these efforts without any assurance that such marketing efforts will yield any substantial revenue stream.

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Moreover, in the event that we cannot identify a replacement licensee by a certain agreed upon date, Meda will have the right, but not the obligation, to demand that the marketing authorizations, and the rights to pursue marketing authorizations, for ONSOLIS® in North America revert back to Meda, with the full reinstatement of all of Meda s rights and obligations under the Meda license. Such reinstatement would be in the full discretion of Meda and we cannot provide any assurance that Meda will exercise its option to reinstate the license. If we cannot find a replacement licensee, and Meda does not choose to reinstate its license, our revenue and results of operations may be adversely affected.

Acceptance of our technologies, product candidates or products in the marketplace is uncertain and failure to achieve market acceptance will prevent or delay our ability to generate material revenues.

Our future financial performance will depend, to a large extent, upon the introduction and physician and patient acceptance of our technologies, product candidates and products. Even if approved for marketing by the necessary regulatory authorities, our technologies, product candidates and products may not achieve market acceptance.

The degree of market acceptance for our products and product candidates will depend upon a number of factors, including:

- regulatory clearance of marketing claims for the uses that we are developing;
- demonstration of the advantages, safety and efficacy of our products and technologies;
- pricing and reimbursement policies of government and third-party payers such as insurance companies, health maintenance organizations and other health plan administrators;
- ability to attract corporate partners, including pharmaceutical companies, to assist in commercializing our products;
- regulatory programs such as the class-wide REMS for ONSOLIS® or market (including competitive) forces that may make it more difficult for us to penetrate a particular market segment; and
- ability to timely and effectively manufacture and market our products.

Physicians, various other health care providers, patients, payers or the medical community in general may be unwilling to accept, utilize or recommend any of our approved products or product candidates. If we are unable to obtain regulatory approval, or are unable (either on our own or through third parties) to manufacture, commercialize and market our proposed formulations or products when planned, we may not achieve any market acceptance or generate revenue.

All of these risks are particularly true for BUNAVAIL®, which will be our first product that we have commercialized ourselves.

If we are unable to convince physicians as to the benefits of our products or product candidates, we may incur delays or additional expense in our attempt to establish market acceptance.

Use of our products and, if approved, our product candidates will require physicians to be informed regarding the intended benefits of our products and product candidates. The time and cost of such an educational process may be substantial. Inability to carry out this physician education process may adversely affect market acceptance of our proposed formulations or products. We may be unable to timely educate physicians regarding our intended pharmaceutical formulations or products in sufficient numbers to achieve our marketing plans or to achieve product acceptance. Any delay in physician education may materially delay or reduce demand for our formulations or products. In addition, we may expend significant funds toward physician education before any acceptance or demand for our products or product candidates are created, if at all. Nonetheless, even with our best efforts, certain physicians may never prescribe our product.

We have been and expect to be significantly dependent on our collaborative agreements for the development, manufacturing and sales of our products and product candidates, which expose us to the risk of reliance on the performance of third parties.

In conducting our research and development activities, we currently rely, and expect to continue to rely, on numerous collaborative agreements with third parties such as manufacturers, contract research organizations, contract sales organizations, commercial partners, universities, governmental agencies and not-for-profit organizations for both strategic and financial resources. Key among these agreements are our commercialization agreement with Endo, our agreements relating to Clonidine Topical Gel and

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Buprenorphine Depot Injection, and our manufacturing development and supply agreements with Aveva, which is expiring on October 15, 2015, and LTS relating to ONSOLIS® and with LTS relating to BREAKYL . For BUNAVAIL®, we have manufacturing and supply arrangements in place.

The termination of these relationships, or failure to perform by us or our partners (who are subject to regulatory, competitive and other risks) under their applicable agreements or arrangements with us, or our failure to secure additional agreements for our product candidates, including a new licensing agreement for marketing rights in North America with respect to ONSOLIS®, would substantially disrupt or delay our research and development and commercialization activities, including our in-process and anticipated clinical trials and commercial sales. Any such loss would likely increase our expenses and materially harm our business, financial condition and results of operation.

The risks associated with reliance on key third parties was demonstrated in 2010 when Aveva experienced certain adverse equipment and regulatory issues leading to the temporary stoppage of manufacturing of all products at that site, which left us exposed to delays in our and our partners commercial plans. In addition, in March 2012 Meda temporarily suspended distribution of ONSOLIS® following discussions with the FDA regarding issues with the product s appearance. Specifically, the FDA raised concerns about two cosmetic issues that may have originated from the formulation used in the manufacturing of ONSOLIS® following an inspection of Aveva, which manufactures ONSOLIS® on our behalf. On March 12, 2012, we announced the postponement of the U.S. and Canadian re-launch of ONSOLIS® until the product formulation can be modified to address these issues. Therefore, ONSOLIS® is not currently being marketed in the U.S. and Canada and the relaunch and additional manufacturing of ONSOLIS® has been postponed until such product issues have been resolved. Any future manufacturing interruptions or related supply issues could have a material adverse effect on our company.

Under our license option agreement with Evonik, we are responsible for paying certain costs relating to the development, formulation and commercialization of buprenorphine for the treatment of opioid dependence. In addition, under our licensing and development agreement with Endo, we are responsible for supporting the clinical development of BELBUCA for pain by conducting certain specified clinical trials in the United States. Our inability to adequately project or control our costs under these agreements could have a material adverse effect on our potential profits from such agreements.

We depend upon key personnel who may terminate their employment with us at any time, and we will need to hire additional qualified personnel.

Our ability to achieve our corporate objectives will depend to a significant degree upon the continued services of key management, technical and scientific personnel, particularly our senior executive officers such as our President and Chief Executive Officer Mark Sirgo. Our management and other employees may voluntarily terminate their employment with us at any time. The loss of the services of these or other key personnel, or the inability to attract and retain additional qualified personnel, could result in delays to product development or approval, loss of sales and diversion of management resources. In addition, we depend on our ability to attract and retain other highly skilled personnel, including research scientists. Competition for qualified personnel is intense, and the process of hiring and integrating such qualified personnel is often lengthy. We may be unable to recruit such personnel on a timely basis, if at all, which would negatively impact our development and commercialization programs. Additionally, we do not currently maintain key person life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

We may be unable to manage our growth effectively.

After focusing our efforts for many years on clinical development of products, our business strategy now contemplates growth and expansion as we continue our evolution into a fully integrated specialty pharmaceutical company. For example, as we in-license or acquire additional product candidates, we will likely have to expand existing operations in order to conduct additional clinical trials, increase our contract manufacturing capabilities, hire and train new personnel to handle the marketing and sales of our products and assist patients in obtaining reimbursement for the use of our products. We may also need to grow to support our commercial activities for BUNAVAIL® or other approved products. This growth may place significant strain on our management and financial and operational resources. Successful growth is also dependent upon our ability to implement appropriate financial and management controls, systems and procedures. Our ability to effectively manage growth depends on our success in attracting and retaining highly qualified personnel, for which the competition may be intense. If we fail to manage these challenges effectively, our business could be harmed.

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We are exposed to product liability, non-clinical and clinical liability risks which could place a substantial financial burden upon us, should lawsuits be filed against us.

Our business exposes us to potential product liability and other liability risks that are inherent in the testing, manufacturing and marketing of pharmaceutical formulations and products. We expect that such claims are likely to be asserted against us at some point. In addition, the use in our clinical trials of pharmaceutical formulations and products and the subsequent sale of these formulations or products by us or our potential collaborators may cause us to bear a portion of or all product liability risks. A successful liability claim or series of claims brought against us could have a material adverse effect on our business, financial condition and results of operations.

We currently have a general liability/product liability policy which includes coverage for our clinical trials and our commercially marketed products. Annual aggregate limits include $2 million for general liability, with $1 million for each occurrence; product liability is $15 million for aggregate and $15 million per occurrence with excess liability in the amount of an additional $5 million; umbrella liability is $5 million aggregate and $5 million per occurrence. It is possible that this coverage will be insufficient to protect us from future claims. Under our agreements, Meda is required to carry comprehensive general product liability and tort liability insurance, each in amounts not less than $2 million per incident and US $10 million annual aggregate and to name us as an additional insured thereon. However, we or our commercial partners may be unable to obtain or maintain adequate product liability insurance on acceptable terms, if at all, and there is a risk that our insurance will not provide adequate coverage against our potential liabilities. Furthermore, our current and potential partners with whom we have collaborative agreements or our future licensees may not be willing to indemnify us against these types of liabilities and may not themselves be sufficiently insured or have sufficient assets to satisfy any product liability claims. Claims or losses in excess of any product liability insurance coverage that may be obtained by us or our partners could have a material adverse effect on our business, financial condition and results of operations.

Moreover, product liability insurance is costly, and due to the nature of the pharmaceutical products underlying ONSOLIS®, BUNAVAIL® and our product candidates, we or our partners may not be able to obtain such insurance, or, if obtained, we or our partners may not be able to maintain such insurance on economically feasible terms. If a product or product candidate related action is brought against us, or liability is found against us prior to our obtaining product liability insurance for any product or product candidate, or should we have liability found against us for any other matter in excess of any insurance coverage we may carry, we could face significant difficulty continuing operations.

We are presently a party to lawsuits by a third parties who claims that our products, methods of manufacture or methods of use infringe on their intellectual property rights, and we may be exposed to these types of claims in the future.

We are presently, and may continue to be, exposed to litigation by third parties based on claims that our technologies, processes, formulations, methods, or products infringe the intellectual property rights of others or that we have misappropriated the trade secrets of others. This risk is exacerbated by the fact that the validity and breadth of claims covered in pharmaceutical patents is, in most instances, uncertain and highly complex. Any litigation or claims against us, whether or not valid, would result in substantial costs, could place a significant strain on our financial and human resources and could harm our reputation. Such a situation may force us to do one or more of the following:

incur significant costs in legal expenses for defending against an intellectual property infringement suit;

delay the launch of, or cease selling, making, importing, incorporating or using one or more or all of our technologies and/or formulations or products that incorporate the challenged intellectual property, which would adversely affect our revenue;

obtain a license from the holder of the infringed intellectual property right, which license may be costly or may not be available on reasonable terms, if at all; or

redesign our formulations or products, which would be costly and time-consuming.

With respect to our BEMA® delivery technology, the drug delivery device technology space is competitive. There is a risk that a court of law in the United States or elsewhere could determine that ONSOLIS® or another of our BEMA® based products is in conflict with or covered by external patents. This risk presently exists in our litigation with MonoSol which was filed by MonoSol in November 2010, wherein MonoSol claims that our and our partner s trade secret manufacturing process for ONSOLIS® is infringing upon MonoSol s patented manufacturing process, as well as a similar litigation with Reckitt Benckiser, Inc., RB Pharmaceuticals Limited, and MonoSol relating to our BUNAVAIL® product which was filed in October 2013. If the courts in these cases were to rule against us and our partner in that case, we could be forced to license technology from MonoSol or otherwise incur liability for damages, which could have a material adverse effect on our ability for us or our partners to market and sell ONSOLIS® or BUNAVAIL®.

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We have been granted non-exclusive license rights to European Patent No. 949 925, which is controlled by LTS to market ONSOLIS® and BELBUCA within the countries of the European Union. We are required to pay a low single digit royalty on sales of products that are covered by this patent in the European Union. We have not conducted freedom to operate searches and analyses for our other proposed products. Moreover, the possibility exists that a patent could issue that would cover one or more of our products, requiring us to defend a patent infringement suit or necessitating a patent validity challenge that would be costly, time consuming and possibly unsuccessful.

Our lawsuit with MonoSol has caused us to incur significant legal costs to defend ourselves, and we would be subject to similar costs if we are a party to similar lawsuits in the future. Furthermore, if a court were to determine that we infringe any other patents and that such patents are valid, we might be required to seek one or more licenses to commercialize our BEMA® products (including, without limitation, ONSOLIS®). We may be unable to obtain such licenses from the patent holders, which could materially and adversely impact our business.

If we are unable to adequately protect or enforce our rights to intellectual property or secure rights to third-party patents, we may lose valuable rights, experience reduced market share, assuming there is any market share, or incur costly litigation to, enforce, maintain or protect such rights.

Our ability to license, enforce and maintain patents, maintain trade secret protection and operate without infringing the proprietary rights of others will be important to our commercializing any formulations or products under development. The current and future development of our drug delivery technologies is contingent upon whether we are able to maintain licenses and access patented technologies. Without these licenses, the use of technologies would be limited and the sales of our products could be prohibited. Therefore, any disruption in access to the technologies could substantially delay the development and sale of our products.

The patent positions of biotechnology and pharmaceutical companies, including ours, which involve licensing agreements, are frequently uncertain and involve complex legal and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued. Consequently, our patents, patent applications and licensed rights may not provide protection against competitive technologies or may be held invalid if challenged or could be circumvented. Our competitors may also independently develop drug delivery technologies or products similar to ours or design around or otherwise circumvent patents issued to, or licensed by, us. In addition, the laws of some foreign countries may not protect our proprietary rights to the same extent as U.S. law.

We also rely upon trade secrets, technical know-how and continuing technological innovation to develop and maintain our competitive position. We require our employees, consultants, advisors and collaborators to execute appropriate confidentiality and assignment-of-inventions agreements with us. These agreements provide that materials and confidential information developed or made known to the individual during the course of the individual s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances and assign the ownership of relevant inventions created during the course of employment to us. These agreements may be breached, and in some instances, we may not have an appropriate remedy available for breach of the agreements. Furthermore, our competitors may independently develop substantially equivalent proprietary information and techniques, reverse engineer, or otherwise gain access to our proprietary technology. We may be unable to meaningfully protect our rights in trade secrets, technical know-how and other non-patented technology.

In addition, we may have to resort to costly and time consuming litigation to protect or enforce our rights under certain intellectual property, or to determine their scope, validity or enforceability. Enforcing or defending our rights will be expensive, could cause significant diversion of our resources and may not prove successful. Any failure to enforce or protect our rights could cause us to lose the ability to exclude others from using our technologies to develop or sell competing products.

We are dependent on third party suppliers for key components of our delivery technologies, products and product candidates.

Key components of our drug delivery technologies, products and product candidates may be provided by sole or limited numbers of suppliers, and supply shortages or loss of these suppliers could result in interruptions in supply or increased costs. Certain components used in our research and development activities, such as the active pharmaceutical component of our products, are currently purchased from a single or a limited number of outside sources. The reliance on a sole or limited number of suppliers could result in:

delays associated with research and development and non-clinical and clinical trials due to an inability to timely obtain a single or limited source component;

inability to timely obtain an adequate supply of required components; and

reduced control over pricing, quality and timely delivery.

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Our relationships with our manufacturers and suppliers are particularly important to us and any loss of or material diminution of their capabilities due to factors such as regulatory issues, accidents, acts of God or any other factor would have a material adverse effect on our company. Such risks were demonstrated when certain manufacturing issues were experienced at Aveva in 2010-2011 and when, subsequently and separately, the FDA identified certain product appearance issues with ONSOLIS®, which resulted in the March 2012 postponement of the U.S. and Canadian relaunch of the product until such issues are resolved. Any loss of or interruption in the supply of components from our suppliers or other third party suppliers would require us to seek alternative sources of supply or require us to manufacture these components internally, which we are currently not able to do.

If the supply of any components is lost or interrupted, product or components from alternative suppliers may not be available in sufficient quality or in volumes within required time frames, if at all, to meet our or our partners needs. This could delay our ability to complete clinical trials, obtain approval for commercialization or commence marketing or cause us to lose sales, force us into breach of other agreements, incur additional costs, delay new product introductions or harm our reputation. Furthermore, product or components from a new supplier may not be identical to those provided by the original supplier. Such differences could have material effects on our overall business plan and timing, could fall outside of regulatory requirements, affect product formulations or the safety and effectiveness of our products that are being developed.

We have limited manufacturing experience and therefore depend on third parties to formulate and manufacture our products. We may not be able to secure or maintain the manufacture of sufficient quantities or at an acceptable cost necessary to successfully commercialize or continue to sell our products.

Our management s expertise has primarily been in the areas of research and development, formulation development and clinical trial phases of pharmaceutical product development. Our management s experience in the manufacturing of pharmaceutical products is more limited and we have limited equipment and no facilities of our own from which these activities could be performed. Therefore, we are fully dependent on third parties for our formulation development, manufacturing and the packaging of our products. This is particularly true with respect to ARx and Sharp, the primary manufacturers of our approved and commercialized product, BUNAVAIL®. We also rely on Aveva, the manufacturer of ONSOLIS® in the U.S., and LTS, the manufacturer for BREAKYL in the E.U. This reliance exposes us to the risk of not being able to directly oversee the production and quality of the manufacturing process and provide ample commercial supplies to formulate sufficient product to conduct clinical trials and maintain adequate supplies to meet market demand for our products.

Furthermore, these third party contractors, whether foreign or domestic, may experience regulatory compliance difficulty, mechanical shut downs, employee strikes, or any other unforeseeable acts that may delay or limit production, which could leave our commercial partners with inadequate supplies of product to sell, especially when regulatory requirements or customer demand necessitate the need for additional product supplies. Our inability to adequately establish, supervise and conduct (either ourselves or through third parties) all aspects of the formulation and manufacturing processes, and the inability of third party manufacturers like ARx, Sharp, Aveva and LTS to consistently supply quality product when required would have a material adverse effect on our ability to commercialize and sell our products.

These risks associated with reliance on key third party manufacturers was demonstrated in March 2012, when Meda temporarily suspended distribution of ONSOLIS® following discussions with the FDA regarding certain appearance issues with the product. Specifically, the FDA raised concerns about two appearance issues with ONSOLIS® following an inspection of Aveva s manufacturing facility. On March 12, 2012, we announced the postponement of the U.S. and Canadian relaunch of ONSOLIS® until the product formulation can be modified to address these issues. Therefore, ONSOLIS® is not currently being marketed in the US and Canada and the relaunch

and additional manufacturing of ONSOLIS® for those jurisdictions has been postponed until such product issues have been resolved. Any future manufacturing interruptions or related supply issues could have an adverse effect on our company, including loss of sales and royalty revenue and claims by or against us or our partners for breach of contract.

There are risks associated with our reliance on third parties for marketing, sales, managed care and distribution infrastructure and channels.

We expect that we will be required to enter into agreements with commercial partners (such as our agreement with Endo) to engage in sales, marketing and distribution efforts around our products and product candidates. This is the case with our current self-commercialization activities with BUNAVAIL®, for which we have contracted with Quintiles to provide our sales force. We may be unable to establish or maintain third-party relationships on a commercially reasonable basis, if at all. In addition, these third parties may have similar or more established relationships with our competitors. If we do not enter into relationships with third parties for the sales and marketing of our proposed formulations or products, we will need to develop our own sales and marketing capabilities.

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We may be unable to engage qualified distributors. Even if engaged, these distributors may:

- fail to satisfy financial or contractual obligations to us;
- fail to adequately market our formulations or products;
- cease operations with little or no notice to us; or
- offer, design, manufacture or promote competing formulations or products.

If we fail to develop sales, managed care, marketing and distribution channels, we would experience delays in generating sales and incur increased costs, which would harm our financial results.

The class-wide Risk Evaluation and Mitigation Strategy (REMS) for all transmucosal fentanyl products, and similar programs for other narcotic products, may continue to slow sales and marketing efforts for ONSOLIS® and our future sales and marketing efforts for future products that contain narcotics, which could impact our royalty and sales revenue from such products.

Our approved product ONSOLIS® is formulated with the potent narcotic fentanyl. On December 29, 2011, FDA approved a REMS program covering all transmucosal fentanyl products. The program, which is referred to as the Transmucosal Immediate Release Fentanyl (TIRF) REMS Access Program, was designed to ensure informed risk-benefit decisions before initiating treatment with a transmucosal fentanyl product, and while patients are on treatment, to ensure appropriate use. The approved program covers all approved transmucosal fentanyl products under a single program and was implemented in March 2012. There is a risk that healthcare providers may respond negatively to this class-wide REMS program in a manner similar to the original ONSOLIS® REMS program that we were required to implement prior to the adoption of the class-wide REMS. Should this occur, our ability (or the ability of potential future commercial partners) to generate revenue from sales of ONSOLIS® in the U.S. and Canada, once the appearance and related formulation issues have been resolved and the product is relaunched in the U.S. and Canada, could be materially compromised, which would result in low payments to us. Additionally, the FDA has implemented a class-wide REMS covering the extended release and long acting opioid class. The class-wide REMS program consists of a REMS-compliant educational program offered by an accredited provider of continuing medical education, patient counseling materials and a medication guide. BELBUCA is anticipated to fall within the existing class-wide REMS program. The cost and implementation of the extended release and long-acting opioid REMS is shared among multiple companies in the category.

There also continues to be a REMS in place for buprenorphine for the treatment of opioid dependence referred to as the BTOD (Buprenorphine-containing Transmucosal products for Opioid Dependence) REMS. BUNAVAIL® falls within the existing REMS, which is far less cumbersome and includes a medication guide and healthcare professional and patient education. Given the existence of a REMS in both the extended release and long-acting opioid and opioid dependence markets, we anticipate our products will fit within the existing REMS and will avoid the issues encountered with ONSOLIS®, where a REMS program was yet to be developed.

BUNAVAIL® is the first product that we have elected to commercialize. If we are unable to adequately develop, implement, or manage our sales, marketing and distribution capabilities, either on our own or through third parties

who perform these functions, our commercialization efforts for BUNAVAIL® or any future product we may commercialize would not produce the desired results, which would hurt our revenues and results of operations.

Prior to our decision to commercialize BUNAVAIL®, we have relied on third parties to manage sales and marketing efforts for us, including Meda for ONSOLIS® and, if BELBUCA is approved, Endo. We therefore have little experience as a company in commercializing a product, and our sales, marketing and distribution capabilities are new. As such, we may not achieve success in marketing and promoting BUNAVAIL®, or any other products we develop or acquire in the future or products we may commercialize through the exercise of co-promotion rights. Specifically, in order to optimize the commercial potential of BUNAVAIL®, we must execute upon our commercialization plan effectively and efficiently. In addition, we must continually assess and modify our commercialization plan in order to adapt to the promotional response. Further, we must continue to focus and refine our marketing campaign to ensure a clear and understandable physician-patient dialogue around BUNAVAIL® as an appropriate therapy. In addition, we must provide our sales force with the highest quality training, support, guidance and oversight in order for them to effectively promote BUNAVAIL®. If we fail to perform these commercial functions in the highest quality manner, BUNAVAIL® will not achieve its maximum commercial potential or any level of success at all. With respect to BUNAVAIL®, we rely on our agreement with Quintiles, who is responsible for providing our sales force on an outsourced basis. Should our relationship with Quintiles deteriorate or if our agreement with Quintiles is terminated, our sales efforts with BUNAVAIL® would likely suffer materially and we may not be able to keep or reconstitute our sales force. In addition, sales and marketing efforts could be negatively impacted by the delay or failure to obtain additional supportive clinical trial data for our products, as is the requirement for BUNAVAIL®. The deterioration or loss of our sales force would materially and adversely impact our ability to generate sales revenue, which would hurt our results of

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operations. Finally, we are competing and expect to compete with other companies that currently have extensive and well-funded marketing and sales operations, and our marketing and sales efforts may be unable to compete against these other companies, which would also hurt our results of operations.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems and those of our current and any future partners, contractors, and consultants are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. System failures, accidents, or security breaches could cause interruptions in our operations, and could result in a material disruption of our commercialization activities, development programs and our business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the commercialization of any potential product candidate could be delayed.

Risks Related to Our Products in Development and Regulation

We depend in large part on our BEMA® drug delivery technology, and the loss of access to this technology would terminate or delay the further development of our products, injure our reputation or force us to pay higher fees.

We depend, in large part, on our BEMA® drug delivery technology. The loss of this key technology would seriously impair our business and future viability, and could result in delays in developing, introducing or maintaining our products and formulations until equivalent technology, if available, is identified, licensed and integrated. In addition, any defects in the BEMA® technology or other technologies we gain access to in the future could prevent the implementation or impair the functionality of our products or formulations, delay new product or formulation introductions or injure our reputation. If we are required to acquire or enter into license agreements with third parties for replacement technologies, we could be subject to higher fees, milestone or royalty payments, assuming we could access such technologies at all.

Our failure to obtain costly government approvals, including required FDA approvals, or to comply with ongoing governmental regulations relating to our technologies and proposed products and formulations could delay or limit introduction of our proposed formulations and products and result in failure to achieve revenues or maintain our ongoing business.

Our research and development activities and the manufacture and marketing of our products and product candidates are subject to extensive regulation for safety, efficacy and quality by numerous government authorities in the United States and abroad. Before receiving FDA or foreign regulatory clearance to market our proposed formulations and products, we will have to demonstrate that our formulations and products are safe and effective in the patient population and for the diseases that are to be treated. Clinical trials, manufacturing and marketing of drugs are subject to the rigorous testing and approval process of the FDA and equivalent foreign regulatory authorities. The Federal Food, Drug and Cosmetic Act and other federal, state and foreign statutes and regulations govern and influence the testing, manufacture, labeling, advertising, distribution and promotion of drugs and medical devices. As a result, regulatory approvals can take a number of years or longer to accomplish and require the expenditure of substantial financial, managerial and other resources.

Moreover, although we received FDA approval for ONSOLIS® and BUNAVAIL®, ONSOLIS® is not currently being marketed in the U.S. and Canada pending resolution of certain appearance and related formulation issues, and we may not receive regulatory approval for any required changes to the ONSOLIS® formulation or of our other product candidates. We may be unable to obtain all required regulatory approvals, and our failure to do so would materially and adversely affect our business, results of operations and viability.

Our failure to complete or meet key milestones relating to the development of our technologies and proposed products and formulations would significantly impair the viability of our company.

In order to be commercially viable, we must research, develop, obtain regulatory approval for, manufacture, introduce, market and distribute formulations or products incorporating our technologies. For each drug that we formulate with our drug delivery technologies, we must meet a number of critical developmental milestones, including:

demonstration of the benefit from delivery of each specific drug through our drug delivery technologies;

demonstration, through non-clinical and clinical trials, that our drug delivery technologies are safe and effective; and

establishment of a viable Good Manufacturing Process capable of potential scale-up.

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The estimated required capital and time-frames necessary to achieve these developmental milestones is subject to inherent risks, many of which may be beyond our control. As such, we may not be able to achieve these or similar milestones for any of our proposed product candidates or other product candidates in the future. Our failure to meet these or other critical milestones would adversely affect the viability of our company.

Conducting and completing the clinical trials necessary for FDA approval is costly and subject to intense regulatory scrutiny as well as the risk of failing to meet the primary endpoint of such trials. We will not be able to commercialize and sell our proposed products and formulations without completing such trials.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. In order to conduct clinical trials that are necessary to obtain approval by the FDA to market a drug product, the FDA requires the submission of an investigational new drug application, or IND. The FDA has 30 days to review the IND and, unless the FDA raises an issue or concern about the clinical trial plan during that time period, the IND becomes effective at the end of that 30 days and sponsors may proceed with their clinical trial plans. The FDA can suspend or terminate clinical trials at any time due to a number of factors, including for safety or efficacy reasons, because we or our clinical investigators did not comply with the FDA s requirements for conducting clinical trials, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If the FDA does not permit us to proceed with our planned clinical trials or the trials are suspended or permanently terminated by us, the FDA or any institutional review boards overseeing the trials, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

In addition, it is our stated intention to seek to avail ourselves of the FDA s 505(b)(2) approval procedure where it is appropriate to do so. Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act permits an applicant to file a NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The applicant may rely upon published literature and the FDA s findings of safety and effectiveness based on certain preclinical testing or clinical studies conducted for an approved product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. If this approval pathway is not available to us with respect to a particular formulation or product, or at all, the time and cost associated with developing and commercializing such formulations or products may be prohibitive and our business strategy would be materially and adversely affected. For example, in September 2012, the FDA received a Citizen Petition requesting that it refuse to file any Section 505(b)(2) NDA or abbreviated new drug application, or ANDA, for buprenorphine/naloxone drugs intended to be applied to the oral mucosal membranes unless such application refers to the sublingual film formulation of Suboxone®, rather than the tablet formulation, as the reference listed drug, or RLD. Our proposed Section 505(b)(2) marketing application for BUNAVAIL® is expected to reference the tablet formulation of Suboxone® rather than the film formulation as the reference listed drug, and the data we have generated has been based off of the tablet formulation of Suboxone®. While the FDA, on February 22, 2013, rejected the Citizen Petition referred to above, we may be faced with similar issues in the future which might require us to conduct additional studies of our product candidates or otherwise face delays and additional costs.

Moreover, we may be required to conduct additional costly and time-consuming clinical studies beyond those that we originally anticipate in the event that our clinical trials fail to meet their primary endpoints or for other reasons, which would render them inadequate to support approval by the FDA. For example, in September 2011, we announced that our Phase 3 clinical trial for BELBUCA did not meet its primary endpoint and therefore we were required to conduct new trials. In our licensing and development agreement with Endo, we are responsible for the conduct of planned clinical studies leading up to the submission of an NDA for BELBUCA . Conducting a new clinical trial in accordance

with the FDA requirements has required significant additional capital, and we will not be able to commercialize and sell our BELBUCA product until we are able to meet our primary endpoints for both trials and obtain subsequent FDA approval.

Data obtained from clinical trials are susceptible to varying interpretations, which could delay, limit or prevent regulatory approvals.

Data already obtained, or data we may obtain in the future, from non-clinical studies and clinical trials do not necessarily predict the results that will be obtained from later non-clinical studies and clinical trials. Moreover, non-clinical and clinical data are susceptible to multiple and varying interpretations, which could delay, limit or prevent regulatory approval. A number of companies in the pharmaceutical industry, including those involved in competing drug delivery technologies, have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. The failure to adequately demonstrate the safety and effectiveness of a proposed formulation or product under development could delay or prevent regulatory clearance of the product candidate,

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resulting in delays to commercialization, and could materially harm our business. In addition, our clinical trials may not demonstrate sufficient levels of safety and efficacy necessary to obtain the requisite regulatory approvals for our drugs, and thus our proposed drugs may not be approved for marketing.

Finally, if any of our clinical trials do not meet their primary endpoints, or for a variety of other reasons, we may be required to conduct additional clinical trials in order to progress development of the subject product. These additional trials would be costly and time-consuming, and would divert resources from other projects. The foregoing risks were evidenced by the failure of our Phase 3 trial for BELBUCA for the treatment of moderate to severe chronic pain to meet its primary endpoint, which we announced September 2011.

We compete with larger and better capitalized companies, and competitors in the drug development or specialty pharmaceutical industries may develop competing technologies or products which outperform or supplant our technologies or products.

Drug companies and/or other technology companies have developed (and are currently marketing in competition with us), have sought to develop and may in the future seek to develop and market mucosal adhesive, encapsulation or other drug delivery technologies and related pharmaceutical products which do and may compete with our technologies and products. Competitors have developed and may in the future develop similar or different technologies or products which may become more accepted by the marketplace or which may supplant our technology entirely. In addition, many of our current competitors are, and future competitors may be, significantly larger and better financed than we are, thus giving them a significant advantage over us.

We and our partners may be unable to respond to competitive forces presently in the marketplace (including competition from larger companies), which would severely impact our business. Moreover, should competing or dominating technologies or products come into existence and the owners thereof patent the applicable technological advances, we could also be required to license such technologies in order to continue to manufacture, market and sell our products. We may be unable to secure such licenses on commercially acceptable terms, or at all, and our resulting inability to manufacture, market and sell the affected products could have a material adverse effect on us.

Our approved product and other product candidates contain narcotic ingredients which are tightly regulated by federal authorities. The development, manufacturing and sale of such products are subject to strict regulation, including the necessity of risk management programs, which may prove difficult or expensive to comply with.

Our FDA approved products, ONSOLIS® and BUNAVAIL® and our lead product candidate, BELBUCA , contain tightly controlled and highly regulated narcotic ingredients. Misuse or abuse of such drugs can lead to physical or other harm. The FDA or the U.S. Drug Enforcement Administration, or DEA, currently impose and may impose additional regulations concerning the development, manufacture, transportation and sale of prescription narcotics. Such regulations include labeling requirements, the development and implementation of risk management programs, restrictions on prescription and sale of these products and mandatory reformulation of our products in order to make abuse more difficult. This is particularly true with respect to the REMS that the FDA required for ONSOLIS®. In addition, state health departments and boards of pharmacy have authority to regulate distribution and may modify their regulations with respect to prescription narcotics in an attempt to curb abuse. Any such current or new regulations may be difficult and expensive for us and our manufacturing and commercial partners to comply with, may delay the introduction of our products, may adversely affect our net sales, if any, and may have a material adverse effect on our results of operations.

The DEA limits the availability of the active ingredients used in ONSOLIS®, BUNAVAIL® and certain of our product candidates and, as a result, our procurement quota may not be sufficient to meet commercial demand or

complete clinical trials.

The DEA regulates chemical compounds as Schedule I, II, III, IV or V substances, with Schedule I substances considered to present the highest risk of substance abuse and Schedule V substances the lowest risk. The active ingredients in our approved product ONSOLIS® (fentanyl) and BUNAVAIL® (buprenorphine) and in our lead product candidate BELBUCA (BEMA® Buprenorphine) are listed by the DEA as Schedule II (ONSOLIS®) and III (BUNAVAIL® and BELBUCA) substances, respectively, under the Controlled Substances Act of 1970. Consequently, their manufacture, shipment, storage, sale and use are subject to a high degree of regulation. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled.

The DEA limits the availability of the active ingredients used in ONSOLIS®, BUNAVAIL® and potentially other of our product candidates and, as a result, our procurement quota of these active ingredients may not be sufficient to complete clinical trials or meet commercial demand. We must annually apply to the DEA for a procurement quota in order to obtain these substances. The DEA may not establish a procurement quota following FDA approval of an NDA for a controlled substance until after DEA reviews and provides for public comment on the labeling, promotion, risk management plan and other documents associated with such product. A

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DEA review of such materials may result in potentially significant delays in obtaining procurement quota for controlled substances, a reduction in the quota issued to us or an elimination of our quota entirely. Any delay or refusal by the DEA in establishing our procurement quota for controlled substances could delay or stop our clinical trials, product launches or sales of products, which could have a material adverse effect on our business and results of operations.

Risks Related to Our Industry

The market for our products and product candidates is rapidly changing and competitive, and new drug delivery mechanisms, drug delivery technologies, new drugs and new treatments which may be developed by others could impair our ability to maintain and grow our business and remain competitive.

The pharmaceutical and biotechnology industries are subject to rapid and substantial technological change. Developments by others may render our technologies, our approved products and our product candidates noncompetitive or obsolete, or we may be unable to keep pace with technological developments or other market factors. Technological competition from pharmaceutical and biotechnology companies, universities, governmental entities and others now existing or diversifying into the field is intense and is expected to increase. Many of these entities (including our competitors with respect to our two approved products, ONSOLIS® and BUNAVAIL®) have significantly greater research and development capabilities, human resources and budgets than we do, as well as substantially more marketing, manufacturing, financial and managerial resources. These entities represent significant competition for us. Acquisitions of, or investments in, competing pharmaceutical or biotechnology companies by large corporations could increase such competitors financial, marketing, manufacturing and other resources.

With respect to our drug delivery technologies, we may experience technical or intellectual property related challenges inherent in such technologies. Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competition. Some of these technologies may have an entirely different approach or means of accomplishing similar therapeutic effects compared to our technologies. Our competitors may develop drug delivery technologies and drugs that are safer, more effective or less costly than our proposed formulations or products and, therefore, present a serious competitive threat to us.

The potential widespread acceptance of therapies that are alternatives to ours may limit market acceptance of our formulations or products, even if commercialized. Many of our targeted diseases and conditions can also be treated by other medication or drug delivery technologies. These treatments may be widely accepted in medical communities and have a longer history of use. The established use of these competitive drugs may limit the potential for our technologies, formulations and products to receive widespread acceptance if commercialized.

If users of our products and product candidates are unable to obtain adequate reimbursement from third-party payers, or if new restrictive legislation is adopted, market acceptance of our proposed formulations or products may be limited and we may not achieve material revenues.

The continuing efforts of government and insurance companies, health maintenance organizations and other payers of healthcare costs to contain or reduce costs of health care may affect our future revenues and profitability, and the future revenues and profitability of our potential customers, suppliers and collaborative partners and the availability of capital. For example, in certain foreign markets, pricing or profitability of prescription pharmaceuticals is subject to government control. In the United States, given recent federal and state government initiatives directed at lowering the total cost of health care, the U.S. Congress and state legislatures will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid systems. While we cannot predict whether any such legislative or regulatory proposals will be adopted, the announcement or adoption of such

proposals and related laws, rules and regulations could materially harm our business, financial conditions, results of operations or stock price. Moreover, the passage of the Patient Protection and Affordable Care Act in 2010, and efforts to amend or repeal such law, has created significant uncertainty relating to the scope of government regulation of healthcare and related legal and regulatory requirements, which could have an adverse impact on sales of our products.

The ability of our company or any partners with which we may enter into a new licensing arrangement to sell ONSOLIS® and our ability to commercialize BUNAVAIL® will depend in part on the extent to which appropriate reimbursement levels for the cost of our proposed formulations and products and related treatments are obtained by governmental authorities, private health insurers and other organizations, such as HMOs. Consumers and third-party payers are increasingly challenging the prices charged for drugs and medical services. Also, the trend toward managed health care in the United States and the concurrent growth of organizations such as HMOs, which could control or significantly influence the purchase of health care services and drugs, as well as legislative proposals to reform health care or reduce government insurance programs, may all result in lower prices for or rejection of our drugs.

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We could be exposed to significant drug product liability claims which could be time consuming and costly to defend, divert management attention and adversely impact our ability to obtain and maintain insurance coverage.

The testing, manufacture, marketing and sale of our proposed drug formulations involve an inherent risk that product liability claims will be asserted against us. All of our clinical trials have been, and all of our proposed clinical trials are anticipated to be conducted by collaborators and third party contractors. We currently have a general liability/product liability policy which includes coverage for our clinical trials and our commercially marketed products. Annual aggregate limits include $2 million for general liability, with $1 million for each occurrence; product liability is $15 million for aggregate and $15 million per occurrence with excess liability in the amount of an additional $5 million; umbrella liability is $5 million aggregate and $5 million per occurrence. It is possible that this coverage will be insufficient to protect us from future claims. Under our agreements, Meda is required to carry comprehensive general product liability and tort liability insurance, each in amounts not less than $2 million per incident and US $10 million annual aggregate and to name us as an additional insured thereon.

Should we decide to seek additional insurance against such risks before our product sales commence, there is a risk that such insurance will be unavailable to us, or if it can be obtained at such time, that it will be available at an unaffordable cost. Even if we obtain insurance, it may prove inadequate to cover claims and/or litigation costs, especially in the case of wrongful death claims. Product liability claims or other claims related to our products, regardless of their outcome, could require us to spend significant time and money in litigation or to pay significant settlement amounts or judgments. Any successful product liability or other claim may prevent us from obtaining adequate liability insurance in the future on commercially desirable or reasonable terms. An inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of our products and product candidates. A product liability claim could also significantly harm our reputation and delay market acceptance of our proposed formulations and products. In addition, although third party partners are required to provide insurance in connection with specific products such partners may face similar insurance related risks.

Our business involves environmental risks related to handling regulated substances which could severely affect our ability to conduct research and development of our drug delivery technology and product candidates.

In connection with our or our partners research and clinical development activities, as well as the manufacture of materials and products, we and our partners are subject to federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens and wastes. We and our partners may be required to incur significant costs to comply with environmental and health and safety regulations in the future. Our research and clinical development, as well as the activities of our manufacturing and commercial partners, both now and in the future, may involve the controlled use of hazardous materials, including but not limited to certain hazardous chemicals and narcotics. We cannot completely eliminate the risk of accidental contamination or injury from these materials. In the event of such an occurrence, we could be held liable for any damages that result and any such liability could exceed our resources.

Government and other efforts to reform the healthcare industry could have adverse effects on our company, including the inability of users of our current and future approved products to obtain adequate reimbursement from third-party payers, which could lead to diminished market acceptance of, and revenues from, such products.

On March 23, 2010, President Obama signed into law the Patient Protection and Affordable Care Act (or the PPACA). The Healthcare and Education Reconciliation Act of 2010 (or the Reconciliation Act), which contains a number of amendments to the PPACA, was signed into law on March 30, 2010. Two primary goals of the PPACA, combined with the Reconciliation Act (which we collectively refer to as the Health Reform Legislation), are to provide for

increased access to coverage for healthcare and to reduce healthcare-related expenses. On June 28, 2012, the United States Supreme Court upheld the constitutionality of the requirement in PPACA that individuals maintain health insurance or pay a penalty.

The Healthcare Reform Legislation contains a number of provisions that are expected to impact our business and operations or those of our commercial partners, including provisions governing enrollment in federal healthcare programs, reimbursement and discount programs and fraud and abuse prevention and control. The impact of these programs on our business is presently uncertain and may have unexpected consequences for our company. For example, expansion of health insurance coverage under the Health Reform Legislation may result in a reduction in uninsured patients and increase in the number of patients with access to healthcare that have either private or public program coverage, and subsequently prescription drug coverage, including coverage for those products currently approved or in development by us or our partners. However, this outcome, along with any other potential benefits of the Health Reform Legislation which could prove a benefit for us or our commercial partners, is uncertain and may not occur.

In addition to the Health Reform Legislation, we expect that there will continue to be proposals by legislators or new laws, rules and regulations at both the federal and state levels, as well as actions by healthcare and insurance regulators, insurance companies, health maintenance organizations and other payers of healthcare costs aimed at keeping healthcare costs down while expanding individual healthcare benefits. Certain of these changes (including, without limitation, those enacted in connection with the federal or state implementation of the Health Reform Legislation) could impose limitations on the prices we or our commercial partners will be able to charge for any of our approved products or the amounts of reimbursement available for these products from governmental

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agencies or third-party payors, or may increase the tax obligations on life sciences companies such as ours. Any or all of these changes (which are presently unclear and subject to potential modification on an ongoing basis) could impact the ability of users of our approved products to obtain insurance reimbursement for the use of such products or the ability of healthcare professionals to prescribe such products, any of which could have a material adverse effect on our revenues (royalty or otherwise), potential profitability and results of operations.

Furthermore, the ability of our company or of future partners of our company with whom we may enter into licensing arrangements to sell ONSOLIS® (once it is reformulated and placed back on the market in the U.S. and Canada) and the Company s ability to commercialize BUNAVAIL® and our product candidates with partners such as Endo or otherwise will depend in part on the extent to which appropriate reimbursement levels for the cost of our proposed formulations and products and related treatments are obtained by governmental authorities, private health insurers, managed care, and other organizations and may all result in lower prices for or rejection of our products, which could further have a material adverse effect on our revenues (royalty or otherwise) and results of operations.

We may also be subject to healthcare laws, regulation and enforcement; our failure to comply with those laws could have a material adverse effect on our results of operations and financial conditions.

Although we currently do not directly market or promote any of our products, we may also be subject to several healthcare regulations and enforcement by the federal government and the states and foreign governments in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Health Insurance Portability and Accountability Act of 1996 (or HIPAA), as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information;

- the federal healthcare programs Anti-Kickback Law, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;

- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;

- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters; and

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment

or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Risks Related to Our Common Stock and Series A Non-Voting Convertible Preferred Stock

Our business is subject to increasingly complex corporate governance, public disclosure, and accounting requirements and regulations that could adversely affect our business and financial results and condition.

We are subject to changing rules and regulations of various federal and state governmental authorities as well as the stock exchange on which our common stock is listed. These entities, including the Public Company Accounting Oversight Board, the Securities and Exchange Commission (or the SEC) and the Nasdaq Capital Market, have issued a significant number of new and increasingly complex requirements and regulations over the course of the last several years and continue to develop additional requirements and regulations in response to laws enacted by Congress, including the Sarbanes-Oxley Act of 2002 and, most recently, the Dodd-Frank Wall Street Reform and Protection Act, or the Dodd-Frank Act.

There are significant corporate governance and executive compensation-related provisions in the Dodd-Frank Act that expressly authorized or required the SEC to adopt additional rules in these areas, such as shareholder approval of executive compensation (say on pay) and proxy access. Our efforts to comply with these requirements are likely to result in an increase in expenses which is difficult to quantify at this time.

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In addition, we are subject to often complex accounting rules and interpretations promulgated by the Financial Accounting Standards Board (including its Emerging Issues Task Force). In 2012, we became engaged in an SEC review process over our accounting (under applicable revenue recognition literature) for payments we received under our license and commercialization with Endo. On February 28, 2013, we announced the conclusion of that review, which led to our adoption of an alternative revenue recognition interpretation and a resulting restatement of our unaudited financial statements for the first three fiscal quarters of 2012. We may be faced with similar issues in the future, and adjustments to or restatements of our financial statements or accounting policies could have a material adverse effect on our public stock price and our reputation.

Our stock price is subject to market factors, and your investment in our securities could decline in value.

Since our initial public offering in June 2002, there has only been a relatively limited public market for our securities and there is a risk that an active trading market in our securities may not be adequately maintained. In addition, the overall market for securities in recent years has experienced extreme price and volume fluctuations that have particularly affected the market prices of many smaller companies. In particular, the market prices of securities of biotechnology and pharmaceutical companies have been extremely volatile, and have experienced fluctuations that often have been unrelated or disproportionate to operating performance of these companies. These broad market fluctuations could result in extreme fluctuations in the price of our securities, which could cause a decline in the value of your securities. These fluctuations, as well as general economic and market conditions, may have a material or adverse effect on the market price of our common stock.

If we cannot meet the NASDAQ Capital Market s continuing listing requirements and NASDAQ rules, NASDAQ may delist our securities, which could negatively affect our company, the price of our securities and your ability to sell our securities.

As of the date of this Report, our shares are listed on the NASDAQ Capital Market. In the future, however, we may not be able to meet the continued listing requirements of the NASDAQ Capital Market and NASDAQ rules, which require, among other things, maintaining a minimum bid price per share of $1.00, minimum stockholders equity of $2.5 million or a minimum market capitalization of $35 million and a majority of independent directors on our board of directors. We have been subject to delisting proceedings and comments by NASDAQ in the past, and during 2011 our stock price declined to levels that put us at risk of not being able to maintain the required minimum bid price or market capitalization levels or both. If we are unable to satisfy the NASDAQ criteria for continued listing, especially at our current stock price levels, our securities could again be subject to delisting. Trading, if any, of our securities would thereafter be conducted in the over-the-counter market, in the so-called pink sheets or on the OTC Bulletin Board. As a consequence of any such delisting, our stockholders would likely find it more difficult to dispose of, or to obtain accurate quotations as to the prices of our securities.

Our Series A Non-Voting Convertible Preferred Stock ranks senior to our common stock in the event of a bankruptcy, liquidation or winding up of our assets.

As of the date of this Report, we currently have issued and outstanding 2,139,000 shares of Series A Non-Voting Convertible Preferred Stock, which we issued in connection with our $40 million financing which closed on December 2012. In the event of our bankruptcy, liquidation or winding up, our assets will be available to pay obligations on our Series A Non-Voting Convertible Preferred Stock in preference to the holders of our common stock.

Executive officers, directors and entities affiliated with them could, due to their collective ownership interests in our company, have a material level of control over us, which could delay or prevent a change in our corporate

control favored by our other stockholders.

As of the date of this Report, our directors, executive officers and affiliated principal stockholders, together with their affiliates, beneficially own, in the aggregate, approximately 10.98% of our outstanding common stock. These figures do not reflect any future potential exercise of outstanding common stock purchase warrants into shares of common stock. The interests of our current officers, directors and affiliated stockholders may differ from the interests of other stockholders. As a result, these current officers, directors and affiliated stockholders could have the ability to exercise substantial influence over all corporate actions requiring stockholder approval, irrespective of how our other stockholders may vote, including the following actions:

approval of certain mergers and other significant corporate transactions, including a sale of substantially all of our assets and material financing transactions;

election of directors;

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adoption of or amendments to stock option plans;

amendment of charter documents; or

issuance of blank check preferred stock.

Additional authorized shares of our common stock and preferred stock available for issuance may adversely affect the market for our common stock.

As of March 12, 2015, there are 52,320,866 shares of common stock issued and 52,305,375 shares of common stock outstanding and there were 2,139,000 shares of Series A Non-Voting Convertible Preferred Stock issued and outstanding. On July 21, 2011, our stockholders approved an amendment to our certificate of incorporation to increase the number of authorized shares of common stock, par value $.001, of our common stock from 45,000,000 to 75,000,000 shares. This increase in our authorized shares of common stock provides us with the flexibility to issue more shares in the future, which might cause dilution to our stockholders. In addition, the total number of shares of our common stock issued and outstanding does not include shares reserved in anticipation of the exercise of outstanding options or warrants. To the extent such options (including options under our stock incentive plan) or warrants are exercised, the holders of our common stock may experience further dilution.

Moreover, in the event that any future financing should be in the form of, be convertible into or exchangeable for, equity securities, and upon the exercise of options and warrants, investors would experience additional dilution. Finally, in addition to the above referenced shares of common stock which may be issued without stockholder approval, we have 5 million shares of authorized preferred stock, of which 2,139,000 shares have been designated as Series A Non-Voting Convertible Preferred Stock. The remaining 2,290,700 shares of preferred stock remain undesignated shares of preferred stock, the terms of which may be fixed by our board of directors. We have issued preferred stock in the past, and our board of directors has the authority, without stockholder approval, to create and issue one or more additional series of such preferred stock and to determine the voting, dividend and other rights of holders of such preferred stock. The issuance of any of such series of preferred stock may have an adverse effect on the holders of common stock.

Shares eligible for future sale may adversely affect the market for our common stock.

We have a material number of shares of common stock underlying securities of our company, the future sale of which could depress the price of our publicly-traded stock. As of March 12, 2015: (i) 3,254,268 shares of common stock are issuable upon exercise of outstanding stock options at a weighted average exercise price of $5.47 per share, (ii) 284 shares of common stock issuable upon exercise of our outstanding warrants at an exercise price of $3.12 per share and (iii) 4,260,370 restricted stock units eligible to be converted shares of our common stock (iv) 2,139,000 shares of Series A preferred eligible to be converted into shares of our common stock. If and when these securities are exercised into shares of our common stock, our shares outstanding will increase. Such increase in our outstanding securities, and any sales of such shares, could have a material adverse effect on the market for our common stock and the market price of our common stock.

In addition, from time to time, certain of our stockholders may be eligible to sell all or some of their shares of common stock by means of ordinary brokerage transactions in the open market pursuant to Rule 144, promulgated under the Securities Act of 1933, as amended, which we refer to herein as the Securities Act, subject to certain limitations. In general, pursuant to Rule 144, after satisfying a six month holding period: (i) affiliated stockholder (or stockholders whose shares are aggregated) may, under certain circumstances, sell within any three month period a

number of securities which does not exceed the greater of 1% of the then outstanding shares of common stock or the average weekly trading volume of the class during the four calendar weeks prior to such sale and (ii) non-affiliated stockholders may sell without such limitations, provided we are current in our public reporting obligations. Rule 144 also permits the sale of securities by non-affiliates that have satisfied a one year holding period without any limitation or restriction. Any substantial sale of our common stock pursuant to Rule 144 or pursuant to any resale report may have a material adverse effect on the market price of our securities.

Furthermore, sales of our common stock by our directors, officers, or employees may occur as a result of sales effected pursuant to predetermined trading plans adopted under the safe-harbor afforded by SEC Rule 10b5-1.

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Our certificate of incorporation and bylaws contain provisions that may discourage, delay or prevent a change in our management team that stockholders may consider favorable.

Our certificate of incorporation, as amended, our amended and restated bylaws (which were adopted in 2010) and Delaware law contain provisions that may have the effect of preserving our current management, such as:

- providing for a staggered board of directors, which impairs the ability of our stockholders to remove our directors at annual or special meetings of stockholders;
- authorizing the issuance of blank check preferred stock without any need for action by stockholders;
- limiting the ability of stockholders to call special meetings of stockholders;
- permitting stockholder action by written consent;
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings;
- requiring a super-majority vote of our stockholders to remove directors of our company; and
- providing that our stockholders may only remove our directors for cause (as defined in our bylaws).

These provisions affect your rights as a stockholder since they permit our board of directors to make it more difficult for common stockholders to replace members of the board or undertake other significant corporate actions. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt to replace our current management team.

The financial and operational projections that we may make from time to time are subject to inherent risks.

The projections that our management may provide from time to time (including, but not limited to, those relating to potential peak sales amounts, product approval, production and supply dates, commercial launch dates, and other financial or operational matters) reflect numerous assumptions made by management, including assumptions with respect to our specific as well as general business, economic, market and financial conditions and other matters, all of which are difficult to predict and many of which are beyond our control. Accordingly, there is a risk that the assumptions made in preparing the projections, or the projections themselves, will prove inaccurate. There will be differences between actual and projected results, and actual results may be materially different from those contained in the projections. The inclusion of the projections in (or incorporated by reference in) this Report should not be regarded as an indication that we or our management or representatives considered or consider the projections to be a reliable prediction of future events, and the projections should not be relied upon as such.

We do not intend to pay dividends on our common stock.

We have never declared or paid any cash dividend on our capital stock. We currently intend to retain any future earnings and do not expect to pay any dividends for the foreseeable future. Therefore, you should not invest in our common stock in the expectation that you will receive dividends.

Our additional financing requirements could result in dilution to existing stockholders.

The additional financings which we have undertaken and which we may in the future require, have and may be obtained through one or more transactions which have diluted or will dilute (either economically or in percentage terms) the ownership interests of our stockholders. Further, we may not be able to secure such additional financing on terms acceptable to us, if at all. We have the authority to issue additional shares of common stock and preferred stock, as well as additional classes or series of ownership interests or debt obligations which may be convertible into any one or more classes or series of ownership interests. We are authorized to issue 75 million shares of common stock and 2,290,700 shares of preferred stock. Such securities may be issued without the approval or other consent of our stockholders.

Item 1B. Unresolved Staff Comments.

None.

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Item 2. Description of Property.

Our executive offices are located in Raleigh, North Carolina. We moved our corporate office to a larger facility in February 2015. The lease, which commenced November 14, 2014 for 89 months, is approximately 12,000 square foot space and has remaining base rent of $2.4 million payable through July, 2022. Rent is payable in monthly installments, and is subject to yearly price increases and increases for our share of common area maintenance costs. The landlord for this space is HRLP Raleigh, L.P. We believe this space is adequate as our principal executive office location.

Item 3. Legal Proceedings.

Readers are advised that the following disclosure regarding our ongoing litigations with MonoSol and Reckitt Benckiser is intended to provide some background and an update on the matter as required by the rules of the SEC. Additional details regarding the past procedural history of the matter can be found in our previously filed periodic filings with the SEC.

Litigation Related To ONSOLIS®

On November 2, 2010, MonoSol filed an action against us and our commercial partners for ONSOLIS® in the Federal District Court of New Jersey (the DNJ) for alleged patent infringement and false marking. We were formally served in this matter on January 19, 2011. MonoSol claims that our manufacturing process for ONSOLIS®, which has never been disclosed publicly and which we and our partners maintain as a trade secret, infringes its patent (United States Patent No. 7,824,588) (the 588 Patent). Of note, the BEMA® technology itself is not at issue in the case, nor is BELBUCA or BUNAVAIL®, but rather only the manner in which ONSOLIS®, which incorporates the BEMA® technology, is manufactured. Pursuant to its complaint, MonoSol is seeking an unspecified amount of damages, attorney s fees and an injunction preventing future infringement of MonoSol s patents.

We strongly refute as without merit MonoSol s assertion of patent infringement, which relates to our confidential, proprietary manufacturing process for ONSOLIS®. On February 23, 2011, we filed our initial answer in this case. In our answer, we stated our position that our products, methods and/or components do not infringe MonoSol s 588 Patent because they do not meet the limitations of any valid claim of such patent. Moreover, in our answer, we stated our position that MonoSol s 588 Patent is actually invalid and unenforceable for failure to comply with one or more of the requirements of applicable U.S. patent law.

On September 12, 2011, we filed a request for inter partes reexamination in the USPTO of MonoSol s 588 Patent demonstrating that all claims of such patent were anticipated by or obvious in the light of prior art references, including several prior art references not previously considered by the USPTO, and thus invalid. On September 16, 2011, we filed in court a motion for stay pending the outcome of the reexamination proceedings, which subsequently was granted due to the results of the USPTO proceedings as described below.

On November 28, 2011, we announced that we were informed by the USPTO that it had rejected all 191 claims of MonoSol s 588 Patent. On January 20, 2012, we filed requests for reexamination before the USPTO of MonoSol s US patent No 7,357,891 (the 891 Patent), and No 7,425,292 (the 292 Patent), the two additional patents asserted by MonoSol, demonstrating that all claims of those two patents were anticipated by or obvious in the light of prior art references, including prior art references not previously considered by the USPTO, and thus invalid.

In February and March 2012, respectively, the USPTO granted the requests for reexamination we filed with respect to MonoSol s 292 and 891 Patents. In its initial office action in each, the USPTO rejected every claim in each patent.

Based on the action of the USPTO on these three patent reexaminations, the court in our case with MonoSol conducted a status conference on March 7, 2012, at which it granted our motion to stay the case pending final outcome of the reexamination proceedings in the USPTO.

As expected, in the 891 Patent and 292 Patent Ex Parte Reexamination proceedings, MonoSol amended the claims several times and made multiple declarations and arguments in an attempt to overcome the rejections made by the USPTO. These amendments, declarations and other statements regarding the claim language significantly narrowed the scope of their claims in these two patents. In the case of the 891 Patent, not one of the original claims survived reexamination and five separate amendments were filed confirming our position that the patent was invalid. Additionally, we believe that arguments and admissions made by MonoSol prevent it from seeking a broader construction during any subsequent litigation by employing arguments or taking positions that contradict those made during prosecution.

A Reexamination Certificate for MonoSol s 891 Patent in its amended form was issued August 21, 2012 (Reexamined Patent No. 7,357,891C1 or the 891C1 Patent). A Reexamination Certificate for MonoSol s 292 Patent in its amended form was issued on July 3, 2012 (Reexamined Patent No. 7,425,292C1 or the 292C1 Patent). These actions by the USPTO confirm the invalidity of the original patents and through the narrowing of the claims in the reissued patents strengthens our original assertion that our products and technologies do not infringe on MonoSol s original patents.

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Inter partes reviews, a new USPTO process to review the patentability of one or more claims of patents, was enacted in September, 2012. As such, on June 12, 2013, despite our previously noted success in the prior ex parte reexaminations for the 292 and 891 Patents, we availed ourselves of this new process and filed requests for inter partes reviews on the narrowed yet reexamined patents, the 292C1 and 891C1 Patents, to challenge their validity and continue to strengthen our position. This inter partes review process allows us to actively participate in the reviews and address any of MonoSol s arguments and representations made during the review process, which heightens our ability to invalidate these patents. On November 13, 2013, the USPTO decided not to institute the two inter partes reviews for the 891C1 and 292C1 Patents. The USPTO s decision was purely on statutory grounds and based on a technicality (in that the IPRs were not filed within what the UPSTO determined to be the statutory period) rather than substantive grounds. Thus, even though the inter partes reviews were not instituted, the USPTO decision preserves our right to raise the same arguments at a later time (e.g., during litigation). Regardless, our assertion that our products and technologies do not infringe the original 292 and 891 Patents and, now, the reexamined 891C1 and 292C1 Patents remains the same.

Importantly, in the case of MonoSol s 588 Patent, at the conclusion of the reexamination proceedings (and its appeals process), on April 17, 2014, the PTAB issued a Decision on Appeal affirming the Examiner s rejection (and confirming the invalidity) of all the claims of the 588 Patent. MonoSol did not request a rehearing by the May 17, 2014 due date for making such a request and did not further appeal the Decision to the Federal Court of Appeals by the June 17, 2014 due date for making such an appeal. Subsequently, on August 5, 2014, the USPTO issued a Certificate of Reexamination cancelling the 588 Patent claims.

Based on our original assertion that our proprietary manufacturing process for ONSOLIS® does not infringe on patents held by MonoSol, and the denial and subsequent narrowing of the claims on the two reissued patents MonoSol has asserted against us while the third has had all claims rejected by the USPTO, we remain very confident in our original stated position regarding this matter. Thus far, we have proven that the original 292 and 891 patents in light of their reissuance with fewer and narrower claims were indeed invalid and the third and final patent, the 588 patent, was invalid as well with all its claims cancelled. Given the outcomes of the 292, 891 and 588 reexamination proceedings, at a January 22, 2015 status meeting, the Court decided to lift the stay and grant our request for the case to proceed on an expedited basis with a Motion for Summary Judgment to dismiss the action. In doing so, the Judge denied MonoSol s request for full litigation proceedings (including, for example, discovery, depositions, *etc.*). We are required to file our motion for summary judgment by March 13, 2015 and based upon the expedited schedule, the Court could issue a decision on our summary judgment motion by the beginning of April, 2015 on the pleadings alone or if an oral hearing is scheduled, soon thereafter. Based upon the outcome from reexaminations and the Court s grant of our request for the proceedings to move directly to a motion for summary judgment, we believe we will prevail and the case will be dismissed. However, if this does not occur and the case proceeds to trial, we will continue to defend this case vigorously and seek a dismissal at trial. Ultimately, whether now with the motion for summary judgment proceedings or later with trial proceedings, we anticipate that MonoSol s claims against us will be rejected.

Litigation Related To BUNAVAIL®

On October 29, 2013, Reckitt Benckiser, Inc., RB Pharmaceuticals Limited, and MonoSol (collectively, the RB Plaintiffs) filed an action against us relating to our BUNAVAIL® product in the United States District Court for the Eastern District of North Carolina for alleged patent infringement. BUNAVAIL® is a drug approved for the maintenance treatment of opioid dependence. The RB Plaintiffs claim that the formulation for BUNAVAIL®, which has never been disclosed publicly, infringes its patent (United States Patent No. 8,475,832) (the 832 Patent).

On May 21, 2014, the Court granted our motion to dismiss. In doing so, the Court dismissed the case in its entirety. The RB Plaintiffs did not appeal the Court Decision by the June 21, 2014 due date and therefore, the dismissal will

stand and the RB Plaintiffs lose the ability to challenge the Court Decision in the future. The possibility exists, however, that the RB Plaintiffs could file another suit alleging infringement of the 832 Patent. If this occurs, based on our original position that our BUNAVAIL® product does not infringe the 832 Patent, we would defend the case vigorously (as we have done so previously), and we anticipate that such claims against us ultimately would be rejected.

On September 20, 2014, based upon our position and belief that our BUNAVAIL® product does not infringe any patents owned by the RB Plaintiffs, we proactively filed a declaratory judgment action in the United States District Court for the Eastern District of North Carolina, requesting the Court to make a determination that our BUNAVAIL® product does not infringe the RB Plaintiffs 832 Patent, US Patent No. 7,897,080 (080 Patent) and US Patent No. 8,652,378 (378 Patent). With the declaratory judgment, there is an automatic stay in proceedings. The RB Plaintiffs may request that the stay be lifted, but they have the burden of showing that the stay should be lifted. For the 832 Patent, the January 15, 2014 IPR was instituted and all challenged claims were rejected for both anticipation and obviousness. For the 080 Patent, all claims remain rejected in an inter partes reexamination and the reexamination is

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currently in the appeals process, with the oral hearing scheduled for November 5, 2014, and we are currently awaiting a decision from the PTAB. For the 378 Patent, an IPR was filed on June 1, 2014, but an IPR was not instituted. However, in issuing its November 5, 2014 decision not to institute the IPR, the PTAB construed the claims of the 378 Patent narrowly. As in prior litigation proceedings, we believe these IPR and the reexamination filings will provide support for maintaining the stay until the IPR and reexamination proceedings conclude. Indeed, given the PTAB s narrow construction of the claims of the 378 Patent, we filed a motion to withdraw the 378 Patent from the case on December 12, 2014. In addition, we also filed a joint motion to continue the stay (with RB Plaintiffs) in the proceedings on the same day. Both the motion to withdraw the 378 Patent from the proceedings and motion to continue the stay were granted.

On September 22, 2014, the RB Plaintiffs filed an action against us (and our commercial partner) relating to our BUNAVAIL® product in the United States District Court for the District of New Jersey for alleged patent infringement. The RB Plaintiffs claim that BUNAVAIL®, whose formulation and manufacturing processes have never been disclosed publicly, infringes its patent (U.S. Patent No. 8,765,167) (167 Patent). As with prior actions by the RB Plaintiffs, we believe this is another anticompetitive attempt by the RB Plaintiffs to distract our efforts from commercializing BUNAVAIL®. We strongly refute as without merit the RB Plaintiffs assertion of patent infringement and will vigorously defend the lawsuit. In this regard, on October 28, 2014, we filed multiple IPR requests on the 167 Patent demonstrating that certain claims of such patent were anticipated by or obvious in the light of prior art references, including prior art references not previously considered by the USPTO, and thus, invalid. On December 12, 2014, we filed a motion to transfer the case from New Jersey to North Carolina and a motion to dismiss the case against our commercial partner. An oral hearing on these motions was set for March 2, 2015, however, the Court has decided to move forward without an oral hearing and we are awaiting their decision. The Court can still ultimately decide to hold an oral hearing later.

Item 4. Mine Safety Disclosures.

Not applicable.

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PART II

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

Our common stock is listed for quotation on the NASDAQ Capital Market under the symbol BDSI . The range of reported high and reported low sales prices per share for our common stock for each fiscal quarter during 2014 and 2013, as reported by the NASDAQ Capital Market, is set forth below.

Quarterly Common Stock Price Ranges

Fiscal Year 2014, Quarter Ended:	**High**	**Low**
March 31, 2014	$ 10.20	$ 5.65
June 30, 2014	$ 12.81	$ 6.71
September 30, 2014	$ 18.48	$ 11.76
December 31, 2014	$ 18.33	$ 11.48

Fiscal Year 2013, Quarter Ended:	**High**	**Low**
March 31, 2013	$ 4.94	$ 3.52
June 30, 2013	$ 5.74	$ 3.86
September 30, 2013	$ 5.55	$ 4.05
December 31, 2013	$ 6.09	$ 4.16

As of March 12, 2015, we had approximately 115 holders of record of our common stock. No cash dividends have been paid on the common stock to date. We currently intend to retain earnings for further business development and do not expect to pay cash dividends in the foreseeable future.

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Securities Authorized for Issuance Under Equity Compensation Plans

The following table indicates shares of common stock authorized for issuance under our 2011 Equity Incentive Plan as of December 31, 2014:

Plan category	Number of securities to be issued upon exercise of outstanding options, warrants and rights [1]	Weighted-average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance
Equity compensation plans approved by security holders	6,045,460	$ 4.32	2,867,530
Equity compensation plans not approved by security holders			
Total	6,045,460	$ 4.32	2,867,530

[1] Includes 2,073,039 shares of common stock underlying options previously granted under our Amended and Restated 2001 Incentive Plan, which are still exercisable despite the fact that such plan expired July 2011.

Performance Graph

The following graph shows a comparison of the five year total cumulative returns of an investment of $100 in cash on December 31, 2009 in (i) our common stock (ii) the Nasdaq Composite Index (iii) the Nasdaq Biotechnology Index and (iv) the NYSE Pharmaceutical Index. All values assume reinvestment of the full amount of all dividends (to date, we have not declared any dividends).

This stock performance graph shall not be deemed filed with the SEC or subject to Section 18 of the Securities Exchange Act, nor shall it be deemed incorporated by reference in any of our filings under the Securities Act of 1933, as amended (the Securities Act).

Comparison of cumulative total return on investment since December 31, 2009:

	12/31/2009	12/31/2010	12/31/2011	12/31/2012	12/31/2013	12/31/2014
BioDelivery Sciences Int l, Inc.	$ 100.00	$ 90.33	$ 20.61	$ 109.67	$ 149.87	$ 305.85
Nasdaq Composite (U.S. Companies)	100.00	116.91	114.81	133.07	184.06	208.71
Nasdaq Biotechnology	100.00	115.01	128.59	169.61	280.89	376.68
NYSE Pharmaceutical	100.00	98.92	107.67	119.52	151.38	172.31

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Item 6. Selected Financial Data.

The statements of operations data and statements of cash flows data for the years ended December 31, 2014, 2013 and 2012 and the balance sheet data as of December 31, 2014 and 2013 have been derived from our audited consolidated financial statements included elsewhere in this annual report. The statements of operations data and statements of cash flows data for the years ended December 31, 2011 and 2010 and the balance sheet data as of December 31, 2012, 2011 and 2010 have been derived from our audited consolidated financial statements not included in this annual report. The following selected financial data should be read in conjunction with our Management s Discussion and Analysis of Financial Condition and Results of Operations and consolidated financial statements and related notes beginning on page F-1 and other financial information included in this Report.

	2014	2013	2012	2011	2010
Statements of Operations Data:					
Total revenue	$ 38,944	$ 11,356	$ 54,542	$ 3,263	$ 3,405
Operating (loss) income	(38,741)	(56,402)	7,062	(26,988)	(16,319)
Net (loss) income	(54,218)	(57,394)	1,652	(23,325)	(13,033)
Diluted net (loss) income per share	(1.12)	(1.51)	0.05	(0.82)	(0.56)
Balance Sheet Data:					
Cash, short-term and long-term investments	$ 70,472	$ 23,176	$ 63,189	$ 10,750	$ 18,209
Total assets	89,311	38,005	75,739	23,645	33,580
Long-term liabilities	4,873	12,545			
Accumulated deficit	(205,531)	(151,313)	(93,919)	(95,572)	(72,246)
Total stockholders equity (deficit)	54,395	(812)	49,777	4,120	9,786
Statements of Cash Flows Data:					
Net cash flows from operating activities	$ (28,833)	$ (60,103)	$ 12,187	$ (23,275)	$ (11,682)

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing elsewhere in this Report. This discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. The actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors, including, but not limited to, those which are not within our control.

Overview

Strategy

We are a specialty pharmaceutical company that is developing and commercializing, either on our own or in partnerships with third parties, new applications of approved therapeutics to address important unmet medical needs using both proven and new drug delivery technologies. We have developed and are continuing to develop pharmaceutical products aimed principally in the areas of pain management and addiction.

Our strategy is to:

Focus our commercial and development efforts in the areas of pain management and addiction within the U.S. pharmaceutical marketplace;

Identify and acquire rights to products that we believe have potential for near-term regulatory approval through the 505(b)(2) approval process, or are already approved;

Market our products through specialty sales teams by primarily focusing on high-prescribing U.S. physicians in pain and addiction; and

We believe this strategy will allow us to increase our revenues, improve our margins and profitability and enhance stockholder value.

Background of Our Company

We were incorporated in the State of Indiana in 1997 and were reincorporated as a Delaware corporation and conducted our initial public offering in 2002. In August 2004, we acquired Arius Pharmaceuticals, the then licensee (and now owner) of our BEMA® drug delivery technology, and July 2006, we licensed commercialization rights in Europe for our lead product; BEMA® based ONSOLIS®, to Meda. In September 2007, we entered into a definitive License and Development Agreement with Meda for ONSOLIS® in the U.S., Canada and Mexico. In January 2012, we entered into a definitive License and Development Agreement with Endo for BELBUCA for chronic pain and in December 2014, we and Endo filed the NDA submission for FDA approval for BELBUCA , which was accepted February 2015. In March 2013, we entered into a definitive Exclusive License Agreement with

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Arcion pursuant to which Arcion agreed to grant to us an exclusive commercial world-wide license, with rights of sublicense, under certain patent and other intellectual property rights related to in-process research and development to develop, manufacture, market, and sell gel products containing clonidine (or a derivative thereof), alone or in combination with other active ingredients, for topical administration for the treatment of PDN and other indications. On July 31, 2013, we submitted the NDA for BUNAVAIL® to the FDA for review, and on June 6, 2014, we announced the FDA approval of BUNAVAIL®, which it launched November 3, 2014.

2014 and Beyond Highlights

On January 23, 2014, we announced positive top-line results from our pivotal Phase 3 efficacy study of BELBUCA in opioid- naive subjects. The locking of the database for the opioid naive study has triggered a $10 million milestone payment from Endo per our licensing agreement.

On February 7, 2014, we entered into a definitive Securities Purchase Agreement with certain institutional investors relating to a registered direct offering of 7,500,000 shares of our common stock, par value $.001 per share. The shares were sold at a price of $8.00 per share, yielding net offering proceeds of $58.2 million.

On June 25, 2014, the database for the pivotal Phase 3 efficacy study of BELBUCA in opioid-experienced patients was locked. The locking of the database triggered a $10 million milestone payment from Endo.

On October 27, 2014, we entered into a definitive Development and Exclusive License Option Agreement with Evonik to develop and commercialize an injectable, extended release, microparticle formulation of buprenorphine for the treatment of opioid dependence.

In September and October 2014, we sold 529,010 and 116,911 shares of common stock, respectively, under our established at-the market offering program for approximate net proceeds of $8.7 million and $1.9 million, respectively.

On December 8, 2014, we announced that we had completed the randomization of all patients in its ongoing initial pivotal Phase 3 clinical trial for Clonidine Topical Gel for the treatment of PDN. We anticipate that topline results of the study will be available by the end of March 2015.

On December 23, 2014, we announced along with Endo the submission of a NDA for BELBUCA (BEMA® Buprenorphine) to the FDA, which was accepted February 23, 2015. BELBUCA is under development for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

On January 27, 2015, we announced that we had entered into an assignment and revenue sharing agreement with Meda to return to us the marketing authorizations for ONSOLIS® for the U.S. and the right to seek

marketing authorizations for ONSOLIS® in Canada and Mexico. Once the NDA has been returned, we will have the right to work directly with the FDA and submit a prior approval supplement that responds to FDA questions and requests and will hopefully lead to the re-introduction of the product. FDA s review of the application may take up to six months; therefore, we could receive a decision before the end of 2015.

Opportunities and Trends

Our franchise currently consists of five products or product candidates, three of which utilize our patented BEMA® drug delivery technology. ONSOLIS® is approved in the U.S., Canada, EU (where it is marketed as BREAKYL) and Taiwan (where it is marketed as PAINKYL), for the management of breakthrough pain in opioid tolerant, adult patients with cancer. The commercial rights to ONSOLIS® are licensed to Meda for all territories worldwide except for Taiwan (licensed to TTY and South Korea (licensed to Kunwha).

The Company s second product using the BEMA® technology is BUNAVAIL® (buprenorphine and naloxone) buccal film, which was approved by the FDA in June 2014 for the maintenance treatment of opioid dependence. The Company is commercializing BUNAVAIL® and launched the product during the fourth quarter 2014. As with all other buprenorphine containing products for opioid dependence, the approval of BUNAVAIL® carries a standard post-approval requirement by the FDA to conduct a study to determine the effect of BUNAVAIL® on QT prolongation (i.e., an abnormal lengthening of the heartbeat). The clinical study results must be reported to the FDA by the end of 2016.

The Company s third product using the BEMA® technology, BELBUCA , is for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. This product is licensed on a worldwide basis to Endo. We and Endo reported positive study results for two pivotal Phase 3 trials for this product in January and July 2014. In August 2014, we announced that, along with Endo, it engaged in a positive pre-NDA meeting with the FDA regarding its BELBUCA product. On December 23, 2014, we announced along with Endo the submission of a NDA for BELBUCA (BEMA® Buprenorphine) to the FDA, which was accepted February 23, 2015.

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Our fourth product is Clonidine Topical Gel, which is currently in Phase 3 development for the treatment of PND, which was licensed from Arcion in March 2013. In June 2014, we announced the completion of patient enrollment for our Phase 3 study of Clonidine Topical Gel. In August 2014, we announced our completion of a pre-specified interim analysis of the ongoing initial pivotal Phase 3 trial for Clonidine Topical Gel.

Our fifth product is Buprenorphine Depot Injection, which is in development as an injectable, extended release, microparticle formulation of buprenorphine for the treatment of opioid dependence, the rights to which we secured when we entered into a definitive development and exclusive license option agreement from Evonik in October 2014.

As we focus on the growth of our existing products and other product candidates, we also continue to position ourselves to execute upon the licensing and acquisition opportunities that will drive our next phase of growth. Our organization is fully committed to this effort, and we believe we will be successful in executing upon our corporate strategy in ways that will drive this future growth.

In order to do so, we will need to continue to maintain our strategic direction, manage and deploy our available cash efficiently and strengthen our alliance and partner relationships. We believe these actions, combined with the experience and expertise of our management team, position us well to drive the future growth of our revenue and income.

We expect to continue research and development of pharmaceutical products and related drug delivery technologies, some of which will be funded by our commercialization agreements. We will continue to seek additional license agreements, which may include upfront payments. We anticipate that funding for the next several years will come primarily from milestone payments and royalties from Meda and Endo, revenues from sales of BUNAVAIL®, potential sale of securities and collaborative research agreements, including those with pharmaceutical companies.

We have a very limited history of commercial operations, having focused the vast majority of our corporate effort on research and development activities. We have, since our founding, received revenue in the form of: (i) contract revenue from Endo related to an upfront, non-refundable payment for a license of our BELBUCA product in 2012 (a portion of which was recorded as deferred revenue that is being recognized as revenue under prevailing revenue recognition rules), (ii) payment from Endo for a certain patent-related milestones (iii) royalty revenue from Meda for sales of BREAKYL and ONSOLIS®, (iv) upfront non-refundable license and milestone payments from Meda in 2007, 2008, 2009 and 2012 (which were initially classified as deferred revenue and subsequently, a substantial amount was reclassified as recognized revenue under prevailing revenue recognition rules), (v) product sales revenue related to BUNAVAIL® sales and (vi) sponsored research revenue from both Endo and Meda. Only the BUNAVAIL® product sales and Breakyl royalty revenues are repeating or predictable. Until recurring revenue from product sales (BUNAVAIL® is the foremost opportunity) becomes a larger portion of our total revenue, we anticipate that our quarterly results of operations will fluctuate significantly for the foreseeable future.

Readers are cautioned that period-to-period comparisons of our operating results should not be relied upon as predictive of future performance. Our prospects must be considered in light of the risks, expenses and difficulties normally encountered by companies that are involved in the development and commercialization of their products and related technologies, particularly companies in new and rapidly changing markets such as pharmaceuticals, drug delivery and biotechnology. For the foreseeable future, we must, among other things, invest in non-clinical and clinical trials of, and seek regulatory approval for and commercialization of, our product candidates, the outcomes of which are subject to numerous risks, many of which are beyond our control. We must also maintain our relationships with our key commercial partners and address regulatory, legal and/or commercial issues and risks that relate to our business from time to time, many of which could impact, perhaps negatively, our planned operations. We may not be able to appropriately address these risks and difficulties.

Critical Accounting Policies and Estimates

Impairment Testing

In accordance with Generally Accepted Accounting Principles (referred to herein as GAAP), goodwill impairment testing is performed at the reporting unit level annually, or more frequently if indicated by events or conditions. We performed an evaluation and determined that there is only one reporting unit. In the course of the evaluation of the potential impairment of goodwill, either a qualitative or a quantitative assessment may be performed. If a qualitative evaluation determines that no impairment exists, then no further analysis is performed. If a qualitative evaluation is unable to determine whether impairment has occurred, a quantitative evaluation is performed. The quantitative impairment test first identifies potential impairments by comparing the fair value of the reporting unit with its carrying value. If the fair value exceeds the carrying amount, goodwill is not impaired. If the carrying value exceeds the fair value, the implied fair value of goodwill is calculated and an impairment is recorded if the implied fair value is less than the carrying amount. The determination of goodwill impairment is highly subjective. It considers many factors both internal and external and is subject to significant changes from period to period. No goodwill impairment charges have resulted from this analysis for 2014, 2013 or 2012.

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An impairment of a long-lived asset other than goodwill is recognized under GAAP if the carrying value of the asset (or the group of assets of which it is a part) exceeds (i) the future estimated undiscounted cash flow from the use of the asset (or group of assets) and (ii) the fair value of the asset (or asset group). In making this impairment assessment, we predominately use an undiscounted cash flow model derived from internal forecasts. Factors that could change the result of our impairment test include, but are not limited to, different assumptions used to forecast future net sales, expenses, capital expenditures, and working capital requirements used in our cash flow models. In the event that our management determines that the value of intangible assets have become impaired using this approach, we will record an accounting charge for the amount of the impairment. No impairment charges have been recorded for other amortizing intangibles in 2014, 2013 or 2012.

Fair market value accounting (derivative liability)

The most significant estimate that could have a material effect on net (loss) gain is the fair market value accounting for our derivative liability. Our derivative liability consists of free standing warrants that are recorded as liabilities due to the registration rights agreements and the requirement for continued effectiveness of the warrants. As a result, the warrants must be recorded as a liability at fair value. The changes in fair value are posted to the derivative (loss) gain in other (loss) income. We utilize the Black-Scholes method to estimate the fair value of our warrants. The three most significant factors in the Black-Scholes calculation are (i) our stock price, (ii) the volatility of our stock price and (iii) the remaining term of the warrants. During the year ending December 31, 2012, a $3.50 increase in the value of our stock was the primary cause of the $5.6 million derivative loss. During the year ending December 31, 2013, we had a lower average remaining term of the warrants, and the Black-Scholes volatility of our stock over this remaining term was relatively low compared to 2012. These two factors lowered the Black-Scholes value of the warrants, even though our stock price increased in 2013 of $1.58. The result was a $0.1 million derivative gain. During the year ending December 31, 2014, a $6.13 increase in the value of our stock was the primary cause of the $13.2 million derivative loss.

Stock-Based Compensation and other stock-based valuation issues (derivative accounting)

We account for stock-based awards to employees and non-employees using Financial Accounting Standards Board Accounting Standards Codification (FASB)(ASC) FASB ASC Topic 718 Accounting for Share-Based Payments, which provides for the use of the fair value based method to determine compensation for all arrangements where shares of stock or equity instruments are issued for compensation. Fair values of equity securities issued are determined by management based predominantly on the trading price of our common stock. The values of these awards are based upon their grant-date fair value. That cost is recognized over the period during which the employee is required to provide service in exchange for the award.

We use the Black-Scholes option pricing model to determine the fair value of stock option and warrant grants. In applying the Black-Scholes option pricing model during 2014, we assumed risk-free interest rates ranging from 1.58% to 1.70%, expected option terms of 5 years (for employee options), a volatility factor ranging from 73.00% to 78.05% and option exercise prices ranging from $5.58 to $16.36. During 2013, we assumed risk-free interest rates ranging from 0.70% to 1.60%, expected option terms of 5 years (for employee options), a volatility factor ranging from 77.59% to 81.65% and option exercise prices ranging from $4.33 to $5.39. During 2012, we assumed risk-free interest rates ranging from 0.62% to 1.02%, expected option terms of 5 years (for employee options), a volatility factor ranging from 81.96% to 83.69% and option exercise prices ranging from $1.78 to $4.72. During all years 2014, 2013 and 2012, we assumed no dividend yield.

We also use the Black-Scholes option pricing model as the primary basis for valuing our derivative liabilities at each reporting date (both embedded and free-standing derivatives). The underlying assumptions used in this determination

are primarily the same as are used in the determination of stock-based compensation discussed in the previous paragraph except contractual lives of the derivative instruments are utilized rather than expected option terms.

Revenue Recognition

Meda License, Development and Supply Agreements

In August 2006 and September 2007, we entered into certain agreements with Meda to develop and commercialize the ONSOLIS® product, a drug treatment for breakthrough cancer pain delivered utilizing the BEMA® technology. The aforementioned agreements relate to the United States, Mexico and Canada (we refer to such agreements as the Meda U.S. Agreements) and to certain countries in Europe (we refer to such agreements as the Meda EU Agreements and we refer to our agreements with Meda collectively as the Meda Agreements). They carry license terms that commence on the date of first commercial sale in each respective territory and end on the earlier of the entrance of a generic product to the market or upon expiration of the patents, which begin to expire in 2020.

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We recognize revenue associated with the Meda Agreements in accordance with GAAP related to multiple deliverables. Our deliverables under the Meda Agreements, including our related rights and obligations, contractual cash flows and performance periods, are more fully described in Note 6 to the accompanying financial statements.

We have determined that upon inception of both the U.S. and EU Meda arrangements all deliverables to each arrangement are to be considered one combined unit of accounting since the fair value of the undelivered license was not determinable and the research and development efforts provided do not have stand-alone value apart from the license. As such, all cash payments from Meda related to these deliverables prior to FDA approval in July 2009 were recorded as deferred revenue. All cash payments from Meda for upfront and milestone payments and research and development services provided are nonrefundable. Upon commencement of the license term (date of first commercial sale in each territory), the license and certain research and development services deliverables were deliverable to Meda. The first commercial sale in the U.S. occurred in October 2009. As a result, $59.7 million of the aggregate milestones and services revenue was recognized as revenue. The first commercial sale in a European country occurred in October 2012. As a result, $17.5 million was recognized as revenue, which included $5.0 million in milestones received during the year ended December 31, 2012. At December 31, 2014, there was remaining deferred revenue of $1.1 million which is related to the Meda research and development services. As time progresses, we will continue to estimate the time required for ongoing obligations, and adjust the remaining deferred revenue accordingly on a quarterly basis.

Upon delivery of the license to Meda, we have determined that each of the undelivered obligations have stand-alone value to Meda as these post-commercialization services encompass additional clinical trials on different patient groups but do not require further product development and these services and product supply obligations can be provided by third-party providers available to Meda. We have also obtained third-party evidence of fair value for the other research and development services and other service obligations, based on hourly rates billed by unrelated third-party providers for similar services contracted by us. We have obtained third-party evidence of fair value of the product supply deliverable based on the outsourced contract manufacturing cost charged to us from the third-party supplier of the product. The arrangements do not contain any general rights of return. Therefore, the remaining deliverables to the arrangements will be accounted for as three separate units of accounting to include (1) product supply, (2) research and development services for the ONSOLIS® product and (3) the combined requirements related to the remaining other service-related obligations due Meda to include participation in committees and certain other specified services. The estimated portion of the upfront payments of approximately $1.0 million (under the Meda U.S. Agreements) and $0.1 million (under the Meda EU Agreements) attributed to these other service-related obligations will be recognized as revenue as services are provided through expiration of the license terms, as defined above.

We have determined that we are acting as a principal under the Meda Agreements and, as such, we will record product supply revenue, research and development services revenue and other services revenue amounts on a gross basis in our consolidated financial statements.

Endo License, Development and Supply Agreements

In January 2012, we entered into the Endo Agreement with Endo pursuant to which we granted to Endo an exclusive commercial world-wide license to develop, manufacture, market and sell our BELBUCA product and to complete U.S. development of such product candidate for purposes of seeking FDA approval.

Pursuant to the Endo Agreement, Endo has obtained all rights necessary to complete the clinical and commercial development of BELBUCA and to sell the product worldwide. Although Endo has obtained all such necessary rights, we have agreed under the Endo Agreement to be responsible for the completion of certain clinical trials regarding BELBUCA (and providing clinical trial materials for such trials) necessary to submit a NDA to the FDA in order to

obtain approval of BELBUCA in the U.S., in each case pursuant to a development plan set forth in the Endo Agreement (as it may be amended pursuant to the Endo Agreement). We are responsible for development activities through the filing of the NDA in the U.S., while Endo is responsible for the development following the NDA submission as well as the manufacturing, distribution, marketing and sales of BELBUCA on a worldwide basis. In addition, Endo is responsible for all filings required in order to obtain regulatory approval of BELBUCA .

Pursuant to the Endo Agreement, we have received (or are expected to receive upon satisfaction of applicable conditions) the following payments (some portion(s) of which will be utilized by us to support our development obligations under the Endo Agreement with respect to BELBUCA):

$30 million non-refundable upfront license fee (earned in January 2012);

$15 million for enhancement of intellectual property rights (earned in May 2012);

$20 million for full database lock for two clinical trials ($10 million earned in January 2014 and $10 million earned in June 2014);

$10 million upon FDA acceptance of the filed NDA (earned February 2015);

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$50 million upon regulatory approval;

up to an aggregate of $55 million based on the achievement of four separate post-approval sales thresholds; and

sales-based royalties in a particular percentage range on U.S. sales of BELBUCA , and royalties in a lesser range on sales outside the United States, subject to certain restrictions and adjustments.

We have assessed our arrangement with Endo and our deliverables thereunder at inception to determine: (i) the separate units of accounting for revenue recognition purposes, (ii) which payments should be allocated to which of those units of accounting and (iii) the appropriate revenue recognition pattern or trigger for each of those payments. The assessment requires subjective analysis and requires management to make judgments, estimates and assumptions about whether deliverables within multiple-element arrangements are separable and, if so, to determine the amount of arrangement consideration to be allocated to each unit of accounting.

At the inception of the Endo arrangement, we determined that the Endo Agreement is a multi-deliverable arrangement with three deliverables: (1) the license rights related to BELBUCA , (2) services related to obtaining enhanced intellectual property rights through the issuance of a particular patent and (3) clinical development services. We concluded that the license delivered to Endo at the inception of the Endo Agreement has stand-alone value. It was also determined that there was a fourth deliverable, the provision of clinical trial material (or CTM). The amounts involved are, however, immaterial and delivered in essentially the same time frame as the clinical development services. Accordingly, we did not separately account for the CTM deliverable, but consider it part of the clinical development services deliverable.

The initial non-refundable $30 million license fee was allocated to each of the three deliverables based upon their relative selling prices using best estimates. The analysis of the best estimate of the selling price of the deliverables was based on the income approach, our negotiations with Endo and other factors, and was further based on management s estimates and assumptions which included consideration of how a market participant would use the license, estimated market opportunity and market share, our estimate of what contract research organizations would charge for clinical development services, the costs of clinical trial materials and other factors. Also considered were entity specific assumptions regarding the results of clinical trials, the likelihood of FDA approval of the subject product and the likelihood of commercialization based in part on our prior agreements with the BEMA® technology.

Based on this analysis, $15.6 million of the up-front license fee was allocated to the license (which was estimated to have a value significantly in excess of $30 million), and $14.4 million to clinical development services (which is inclusive of the cost of CTM). Although the intellectual property component was considered a separate deliverable, no distinct amount of the up-front payment was assigned to this deliverable because we determined the deliverable to be perfunctory. The amount allocated to the license was recognized as revenue in fiscal year 2012. The portion of the upfront license fee allocated to the clinical development services deliverable of $14.4 million is being recognized as those services are performed. We estimate that such clinical development services will extend into the first half of 2015. Based on the estimated proportion of those services performed, $2.5 million, $6.3 million and $5.2 million was recognized as contract revenue in fiscal years, 2014, 2013 and 2012, respectively, in the accompanying condensed consolidated statements of operations. As a result, $0.4 million remains deferred at December 31, 2014.

We concluded that each of the performance based milestones are substantive and, therefore, revenue has and will be recognized when milestones are earned.

The term of the Endo Agreement shall last, on a country-by-country basis, until the later of: (i) 10 years from the date of the first commercial sale of BELBUCA in a particular country or (ii) the date on which the last valid claim of our patents covering BELBUCA in a particular country has expired or been invalidated. The Endo Agreement shall be subject to termination by Endo, at any time, upon a specific timeframe of prior written notice to us and under certain other conditions by either party as specified in the Endo Agreement.

The remaining milestone payments are expected to be recognized as revenue as they are achieved, except that one milestone is contingently refundable for a period of time. Revenue related to such contingently refundable milestone is expected to be recognized as refund provisions, as defined in the agreement, expire. Sale threshold payments and sales-based royalties will be recognized as they accrue under the terms of the Endo Agreement.

We are reimbursed by Endo for certain contractor costs when these costs go beyond set thresholds as outlined in the Endo Agreement. Endo reimburses us for this spending at cost and we receive no mark-up or profit. The gross amount of these reimbursed research and development costs are reported as research and development reimbursement revenue in the accompanying consolidated statements of operations. We act as a principal, have discretion to choose suppliers, bear credit risk and may perform part of the services required in the transactions. Therefore, these reimbursements are treated as revenue to us. The actual expenses creating the reimbursements are reflected as research and development expense.

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Product Royalty Revenues

Product royalty revenue amounts are based on a percentage of net sales revenue of the ONSOLIS® product under our license agreement with Meda. Product royalty revenues are computed on a quarterly basis when revenues are fixed or determinable, collectability is reasonably assured and all other revenue recognition criteria are met. This is shown as product royalty revenues on the accompanying consolidated statements of operations. Meda has the right to reject products that do not comply with product, packaging, or regulatory specifications. Defective product must be identified by Meda within 10 days after inspection at Meda s distribution site. We bill Meda immediately upon receipt by Meda of product (FOB manufacturer). On a quarterly basis, a reconciliation is prepared that reflects the difference between actual net sales by Meda multiplied by the royalty percentage, and the actual royalty payments made during the quarter (which is based on a transfer price at the time we invoice Meda). The parties true-up the differences within 45 days of each quarter-end.

Product Sales

Product sales amounts relate to sales of BUNAVAIL® which was launched in November 2014. These sales are recognized as revenue when prescriptions are filled. This is shown as product sales on the accompanying consolidated statements of operations.

Research Revenues

Research revenue amounts are recognized as revenue under various contractor agreements with third parties. This is shown as research fees on the accompanying consolidated statements of operations.

Contract Revenue

In each of 2014 and 2013, we recognized as revenue $0.2 million in previously deferred revenue related to our agreement with Meda associated with ONSOLIS®. In 2012, we recognized as revenue $17.5 million in previously deferred revenue as a result of the E.U. launch of BREAKYL . In 2013, we received and recognized as revenue $0.3 million which related to our license agreement with TTY.

Research and Development Reimbursements

Reimbursable revenue amounts are related to certain research and development expenses that are reimbursable from Endo related to the Buprenorphine chronic pain program. Our contract with Endo