BIODELIVERY SCIENCES INTERNATIONAL INC
Form 10-K
March 19, 2012
Table of Contents

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, 2011

¨ **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.)**

801 Corporate Center Drive, Suite #210

Raleigh, NC	**27607**
(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 $.0001	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. ¨

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. ¨

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 ¨
Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company x

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, 2011 was approximately $78,773,615 based on the closing sale price of the company s common stock on such date of $3.23 per share, as reported by the NASDAQ Capital Market.

As of March 13, 2012, there were 29,577,146 shares of company common stock issued and 29,561,655 shares of company common stock outstanding.

Table of Contents

BioDelivery Sciences International, Inc.

Annual Report on Form 10-K

For the fiscal year ended December 31, 2011

TABLE OF CONTENTS

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

Table of Contents

CAUTIONARY NOTE ON FORWARD LOOKING STATEMENTS

This Annual Report on Form 10-K, including the documents referred to or incorporated by reference in this Report or statements of our management referring to our summarizing the contents of this Report, includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. We have based these forward-looking statements on our current expectations and projections about future events. Our actual results may differ materially or perhaps significantly from those discussed herein, or implied by, these forward-looking statements. Forward-looking statements are identified by words such as believe, expect, anticipate, intend, estimate, plan, project and c similar expressions. In addition, any statements that refer to expectations or other characterizations of future events or circumstances are forward-looking statements. Forward-looking statements included in this Report or our other filings with the U.S. Securities and Exchange Commission, or SEC, include, but are not necessarily limited to, those relating to:

- our plans and expectations regarding the timing and outcome of research, development, commercialization, manufacturing, marketing and distribution efforts relating to our BEMA® drug delivery technology platform and any proposed products, product candidates or marketed products, including our sole approved and marketed product, ONSOLIS®, and our partnered product candidate, BEMA® Buprenorphine;

- 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 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;

- 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, or 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 or other claims or disputes relating to our business, technologies, products or processes;

our expected revenues (including sales, milestone payment 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.

Table of Contents

The foregoing does not represent an exhaustive list of matters that may be covered by the forward-looking statements contained herein or risk factors that we are faced with that may cause our actual results to differ from those anticipate in our forward-looking statements. Please see Risk Factors for additional risks which could adversely impact our business and financial performance. Moreover, new risks regularly emerge and it is not possible for our management to predict or articulate all risks we face, 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 of this Report. 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 above and throughout this Report.

Table of Contents

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 proven 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 oncology supportive care. We were incorporated in the State of Indiana in 1997 and were reincorporated as a Delaware corporation in 2002.

In formulating our products and product candidates, we utilize the novel, patent protected and proprietary *BioErodible MucoAdhesive (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 pipeline of product candidates, utilize our BEMA® technology.

We have worked with other delivery technologies in the past, and as part of our corporate growth strategy, we may seek to acquire or license additional drug delivery technologies. Should we gain access to such technologies, we would seek to formulate these technologies with proven, FDA approved therapeutics and utilize our development and commercialization experience to, either by ourselves or through commercial 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 technologies. 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.

ONSOLIS®

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® will be 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. will result in a milestone payment of $2.5 million from Meda. A second milestone payment of $2.5 million will be realized at the time of first commercial sale in the E.U. Both of these milestones are anticipated to occur in 2012. We began receiving royalties from Meda on net sales of ONSOLIS® in the U.S. and Canada following launch and we anticipate additional royalty sales following launch in the E.U. in 2012. Our royalty revenue from this product remains below original projections due to certain regulatory conditions in the U.S., which are discussed below.

We have 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 has an experienced, well trained and highly regarded sales force with a focus in specialty therapeutic areas including pain, allergy and central nervous system conditions. Meda has established a track record of successfully commercializing products. Meda has 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.

Table of Contents

In 2010, we secured commercialization rights for ONSOLIS® for the remaining worldwide territories through execution of licensing agreements with Kunwha Pharmaceutical Ltd. for South Korea and TTY Biopharm Ltd. for Taiwan.

The following is a summary of the current regulatory and commercial Status of ONSOLIS®/BREAKYL .

Region	Partner	Regulatory Status	Commercial Status
U.S.	Meda Pharmaceuticals	Approved	Launched October 2009
Canada	Meda Valeant Pharma Canada Inc.	Approved	Launched 3Q 2011
E.U.	Meda	Approved	Launch anticipated in 2012
Australia	Meda Valeant Pharma Canada Inc.	Filed	
Taiwan	TTY Biopharm Ltd.	Filed	
South Korea	Kunwha Pharmaceutical Co. Ltd.	Pre-registration	

Although we have generated licensing-related and other revenue to date, we have only recently begun to generate revenue from the commercial sales of an approved product ONSOLIS® and 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 manufacturing and formulation issues described below. The lack of approved REMS programs for our direct competitors resulted in an unlevel playing field, which created an unfavorable selling environment for ONSOLIS®. Furthermore, increasing pressure from payers and the availability of generic competitors have further impacted the market.

In December of 2010, Meda submitted to the FDA a new REMS program which was to provide broader access to ONSOLIS® through retail pharmacies and reduce some of the burdens placed on prescribers. This REMS program followed the guidelines provided by the FDA in November 2010, to all companies that were or would be marketing transmucosal fentanyl products, thereby providing for a level playing field. However, the FDA abandoned individual REMS programs through the creation of a consortium consisting of all manufacturers of transmucosal fentanyl products, including both us and our commercial partner Meda. 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 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 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 ends the disparity in prescribing requirements for ONSOLIS® compared to similar products and provides ONSOLIS® with both retail and inpatient facility access. Healthcare professionals and patients enrolled in the prior ONSOLIS® REMS will be automatically transferred into the new TIRF REMS Program. Additionally, prescribers and patients enrolled in other individuals REMS programs will also automatically be transferred into the program. In addition to consistency in educational materials, technological advances will simplify the process of participation and verification of program participation. The full program is expected to be implemented in March 2012. At that point, it is anticipated that ONSOLIS® will be in a better position to compete on its own merits.

On March 12, 2012, we announced the postponement of the U.S. relaunch of ONSOLIS® until the product formulation can be modified to address two appearance issues raised by FDA following a recent inspection of the manufacturing facility of our North American manufacturing partner for ONSOLIS®, Aveva Drug Delivery Systems, Inc. (which we refer to herein as Aveva). Specifically, the FDA identified the formation of microscopic crystals and a slight fading of the color during the 24-month shelf life of the product. While these changes do not affect the product s underlying integrity or safety, the FDA believes that the fading of the color in particular may potentially confuse patients, necessitating a modification of the product and product specification before additional product can be manufactured and distributed. Therefore, the U.S. relaunch and additional manufacturing of ONSOLIS® has been postponed until such product appearance issues have been resolved.

Table of Contents

BEMA® Buprenorphine

Our next product, currently in development, is BEMA® Buprenorphine, a potential treatment for moderate to severe chronic pain. In December 2009, we announced that the primary efficacy endpoint was achieved in a Phase 2 clinical study evaluating the safety and efficacy of a range of doses of BEMA® Buprenorphine. Completion of this Phase 2 study led to the initiation of a Phase 3 double-blind, randomized, placebo-controlled clinical study which was initiated in the fourth quarter of 2010. On September 28, 2011, we announced the preliminary findings of our randomized, placebo-controlled, Phase 3 clinical study of BEMA® Buprenorphine for the treatment of moderate to severe chronic pain in a mixed opioid naïve and opioid experienced population. The primary endpoint of the study, overall pain intensity difference between BEMA® Buprenorphine and placebo, was not achieved. Following full analysis of the data, we concluded that we encountered a high placebo response in the opioid naïve segment of the patient population, particularly at our starting dose, which we believe accounted for the lack of statistically significant efficacy that was observed in the trial overall. This is an occurrence typical of many pain trials, and we feel this can be addressed in future studies with adjustments to our patient population, study criteria, starting dose and sample size. We believe the totality of the study results favor BEMA® Buprenorphine, including a near statistically significant difference between BEMA® Buprenorphine and placebo in the opioid experienced group of patients in the trial (p=0.067). In addition, when eliminating the group of patients that did not titrate beyond the starting dose, a statistically significant difference between BEMA® Buprenorphine and placebo (p=0.025) was identified. Neither of these subgroups was sufficiently large enough to be powered to show a statistical difference; however, the robust results in these subgroups resulted in near statistical significance in the opioid experienced patients and statistical significance in the opioid experienced patients titrating beyond the starting dose. Overall, the trial, though not successful, has provided a wealth of knowledge that will assist us in the final design of what we believe will be successful future clinical studies.

We believe that our outlook on BEMA® Buprenorphine was validated when, in January 2012, we announced the signing of a worldwide licensing and development agreement for BEMA® Buprenorphine with Endo Pharmaceuticals, Inc. (which we refer to herein as Endo) under which we granted to Endo the exclusive, worldwide rights to develop and commercialize BEMA® Buprenorphine for the treatment of chronic pain. The financial terms of our agreement with Endo include: (i) a $30 million upfront payment, 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; (iii) $55 million in potential sales milestones upon achievement of designated sales levels; and (iv) a tiered, mid- to upper-teen royalty on net sales of BEMA® Buprenorphine in the United States and a mid- to high-single digit royalty on net sales of BEMA® Buprenorphine outside the United States. We expect to use portions of our Endo milestone payments to fund our development obligations under the Endo agreement with respect to BEMA® Buprenorphine.

One of the key intellectual property milestones under our Endo agreement was achieved when, in February 2012, 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 is granted, will extend the exclusivity of the BEMA® drug delivery technology for BEMA® Buprenorphine (as well as BEMA® Buprenorphine/Naloxone, discussed below) from 2020 to 2027. As a result, we will be entitled to a milestone payment in the amount of $15 million upon the final granting of this patent and an additional milestone payment of $20 million at the time of approval of a New Drug Application (or NDA) by the FDA for BEMA® Buprenorphine for the treatment of chronic pain.

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 opioids. Endo currently has approximately 650 sales representatives covering pain specialty and primary care physicians. Endo s current branded pain portfolio exceeds $2 billion in annual sales and includes products such as Opana ER, Lidoderm and Voltaren Gel. Endo has strong sales and marketing capability in pain therapeutics, and a managed care organization that has established solid formulary positioning for the company s products. We believe BEMA® Buprenorphine is an excellent fit to Endo s pain portfolio and will, if approved, add a Schedule III opioid to their branded pain franchise. BEMA® Buprenorphine 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, BEMA® Buprenorphine 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).

Table of Contents

BEMA® Buprenorphine/Naloxone

In addition, we believe that the widespread use of buprenorphine for the treatment of opioid dependence presents an additional commercial opportunity for the product, and we are developing a formulation of BEMA® Buprenorphine specifically for the treatment of opioid dependence. The product will combine a high dose of buprenorphine along with an abuse deterrent agent, naloxone. A BEMA® Buprenorphine/Naloxone product would provide us with an opportunity to compete in a rapidly growing opioid dependence market which, according to Wolters Kluwer, currently exceeds $1.4 billion in annual sales in the U.S.

Pharmacokinetic studies have demonstrated the ability of the BEMA® technology to deliver the high doses of buprenorphine necessary for the treatment of opioid dependence. In March 2011, we announced the positive outcome of a pre-Investigational New Drug (pre-IND) meeting with the FDA on the development program for BEMA® Buprenorphine/Naloxone, at which we confirmed that the 505(b)(2) regulatory pathway will be pursued for the clinical development of this product. In September 2011, we announced positive preliminary results from a study assessing the pharmacokinetics of a BEMA® Buprenorphine/Naloxone combination. The study assessed buprenorphine and naloxone absorption profiles compared to the FDA approved and currently marketed opioid dependence product, Suboxone. Results of the study demonstrated the ability of the BEMA® formulation to meet the key pharmacokinetic goal of delivering plasma concentrations of buprenorphine in the range needed to treat opioid dependence while minimizing the exposure of naloxone. In December 2011, we announced positive results of a second pharmacokinetic study and plans to meet with FDA to confirm the development plan and regulatory strategy going forward. A meeting was held with FDA in early February 2012, and following the meeting, we announced that we had reached an agreement with the FDA on the development plan for BEMA® Buprenorphine/Naloxone, which includes a pivotal pharmacokinetic study comparing BEMA® Buprenorphine/Naloxone to Suboxone in normal volunteers and a supporting safety study in opioid dependent patients. The FDA concurred with our strategy while requesting one additional, non-comparative pharmacokinetic study examining the effects of multiple films administered concurrently. A similar study was requested and completed as part of the NDA for ONSOLIS®. We plan to initiate a pivotal bioequivalence study and safety study by mid-2012. Based on current timelines, we believe we may be in a position to submit a NDA in the first half of 2013.

ONSOLIS ® and our product candidates such as BEMA® Buprenorphine may also have broader indications. When presented with viable commercial opportunities for broader indications of our products, we will consider developing the product for those uses. We also continue to explore the use of the BEMA® technology with additional pharmaceutical products that may fulfill an unmet medical need.

Additional Overview Information

From our inception through December 31, 2011, we have recorded accumulated losses totaling approximately $95.6 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 ONSOLIS® and other of our candidate products;
- partnering with other pharmaceutical companies such as Meda and Endo to assist in the distribution of our products for which we would expect to receive upfront milestone and royalty payments;
- licensing and joint venture arrangements with third parties, including other pharmaceutical companies whose own proprietary pharmaceutical products may benefit from our drug delivery technologies, or where their product profile would be augmented by the inclusion of our products; and
- securing proceeds from public and private financings and other strategic transactions.

4

Table of Contents

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 Investigational New Drug Applications (known as INDs) or New Drug Applications (known as NDAs) with the FDA or other regulatory authorities, our estimates of development costs, our projected sales and similar metrics regarding ONSOLIS®, BEMA® Buprenorphine, BEMA® Buprenorphine/Naloxone 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.

Our Drug Delivery Technologies

BEMA® Technology

Our BioErodible MucoAdhesive (known as 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, such as nausea and vomiting.

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 mucosa in seconds and dissolve in minutes;
- 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). For a description of our previous agreements with Tolmar, see Key Collaborative and Supply Agreements below.

Bioral® Technology

We have previously engaged in development efforts with another drug delivery technology, known as the Bioral® technology, although we are not presently (and did not in 2011) dedicate any time or resources to the development of this technology or any related products. The Bioral® technology seeks to encapsulate a selected drug or therapeutic in a crystalline structure termed a cochleate cylinder. All of the components of the cochleate cylinder are naturally occurring substances. The Bioral® drug delivery technology was developed in collaboration with the University of Medicine and Dentistry of New Jersey, which we refer to herein as UMDNJ, and the Albany Medical College (which we refer to herein, collectively with UMDNJ, as the Universities), each of which has granted us the exclusive worldwide licenses under applicable patents.

Table of Contents

ONSOLIS® and Our BEMA® 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
BEMA® Fentanyl ONSOLIS®/BREAKYL (U.S./EU trade names)	Breakthrough cancer Pain in opioid tolerant patients	Approval: U.S. in July 2009; Canada in May 2010; E.U. in October 2010	Partnered worldwide with Meda AB
BEMA® Buprenorphine	Moderate to severe chronic pain	Phase 3 results announced September 2011	Partnered worldwide with Endo Pharmaceuticals
BEMA® Buprenorphine/Naloxone	Treatment of opioid dependency	Pivotal studies planned for 2012; NDA filing anticipated first half 2013	In-house commercialization or partnership.
BEMA® Granisetron	Prevention of nausea and vomiting associated with cancer therapies	IND filing February 2011	In-house commercialization for specialty indications possible; primary care rights expected to be partnered

While continuing to work closely with Meda on ONSOLIS® (including on regulatory approvals in the E.U. and other worldwide jurisdictions (except for Taiwan where we are working with TTY and in South Korea where we are working with Kunwha)), we are presently dedicating much of our corporate resources to developing our pipeline of BEMA® products, particularly BEMA® Buprenorphine and BEMA® Buprenorphine/Naloxone. Depending on the availability of corporate resources and market opportunities, we may elect to accelerate or scale back funding for the development of other programs such as BEMA® Granisetron or other opportunities that we may identify.

BEMA® Formulated Products and Product Candidates

ONSOLIS®

Approved by the FDA in July 2009 and commercially launched in October 2009, ONSOLIS® (fentanyl buccal soluble film) is an approved treatment for the management of breakthrough pain (pain that breaks through the effects of other medications being used to control persistent pain) in patients with cancer, eighteen years of age and older, who are already receiving, and who are tolerant to, opioid therapy for their underlying persistent cancer pain. ONSOLIS® is a formulation of the narcotic fentanyl delivered through our BEMA® technology.

We have granted commercialization and distribution rights for ONSOLIS® on a worldwide basis (except in South Korea and Taiwan) to Meda. Under our agreements with Meda, we receive a double digit royalty on the net sales of ONSOLIS® and also have the potential to receive milestone payments based on achieving certain predetermined sales targets. In May 2010, ONSOLIS® was approved by the Canadian regulatory authorities. ONSOLIS® is marketed in Canada by Meda Valeant Pharma Canada, Inc., a joint venture between Meda and Valeant Canada Limited. Approval was also obtained in the E.U. in October 2010, where the product will be marketed by Meda under the tradename BREAKYL . In May 2010, we announced a commercialization and supply agreement with Kunwha Pharmaceutical Co. Ltd., for BEMA® Fentanyl in South Korea, and in October 2010, a licensing agreement was secured with TTY Biopharm Co. Ltd., for exclusive rights to develop and commercialize the product in Taiwan. These licensing deals provide the opportunity for ONSOLIS®/BREAKYL to be commercialized in all regions globally.

Table of Contents

In 2011, the leading company in the fast-acting fentanyl market was Teva Pharmaceuticals (NASDAQ:TEVA), which completed an acquisition of Cephalon, Inc. in October 2011. Teva markets both the branded (Actiq®) and generic formulations of fentanyl transmucosal lozenge. Additional generic manufacturers include Covidien and Watson Pharmaceuticals. Teva introduced a second transmucosal fentanyl product, Fentora® in late 2006. The reported combined retail sales of these products in 2011 was $346 million. In 2011, additional transmucosal formulations of fentanyl were launched and/or approved, including, Abstral®, a sublingual tablet, which was launched in early 2011 by Prostrakan, a nasal spray formulation from Archimedes sold under the trade name Lazanda® and a sublingual spray from Insys, known as Subsys was approved in January 2012. We believe that ONSOLIS® may offer advantages over the marketed and pipeline fentanyl products in terms of ease of use and other attributes; however, we recognize the substantial increase in competition in the category.

We may at some point pursue an expanded indication that would permit promotion of ONSOLIS® for breakthrough pain in non-cancer patients in partnership with Meda. If obtained, we expect that an expanded claim for use in non-cancer breakthrough pain would increase sales for ONSOLIS®.

BEMA® Buprenorphine (chronic pain)

This product candidate utilizes the BEMA® technology to deliver the opioid analgesic buprenorphine (low dose) for the treatment of moderate to severe chronic pain. Buprenorphine is a marketed opioid analgesic which has comparable efficacy to morphine but with a lower propensity for abuse and addiction and fewer typical opioid side effects. The lower potential for abuse and addiction places BEMA® Buprenorphine as a Schedule III controlled substance versus the majority of the other potent opioids, such as morphine and oxycodone, which are Schedule II. We believe that this attribute will help create a broader market opportunity for BEMA® Buprenorphine as many doctors are, for fear of addiction, reluctant to prescribe narcotics, particularly on a chronic basis. Also, since buprenorphine is a Schedule III controlled substance, physicians will be able to phone, fax or otherwise electronically deliver the prescription to the pharmacy with refills permitted for up to 6 months, thus making chronic therapy easier for both the patient and the physician. Refills are not permitted for Schedule II controlled substances, requiring the patient to obtain a new prescription from the doctor s office and take such prescription to the pharmacy each time the medication is required.

We announced the preliminary findings in September 2011 of our randomized, placebo-controlled, Phase 3 clinical study for the treatment of moderate to severe chronic pain in a mixed opioid naïve and opioid experienced population. The primary endpoint of the study, overall pain intensity difference between BEMA® Buprenorphine and placebo, was not achieved. Following full analysis of the data, we witnessed a high placebo response in the opioid naïve segment of the patient population, particularly at our starting dose, which accounted for the overall lack of efficacy that was observed in the trial overall. We believe the totality of the study results favor BEMA® Buprenorphine, including a near statistically significant difference between BEMA® Buprenorphine and placebo in the opioid experienced group of patients in the trial (p=0.067). In addition, when eliminating the group of patients that did not titrate beyond the starting dose, a statistically significant difference between BEMA® Buprenorphine and placebo (p=0.025) was identified. Neither of these subgroups was sufficiently large enough to be powered to show a statistical difference; however, the robust results in these subgroups resulted in near statistical significance in the opioid experienced patients and statistical significance in the opioid experienced patients titrating beyond the starting dose. We expect to model our future clinical trials for this product with the knowledge gained from our initial Phase 3 study.

In January 2012, we announced the signing of a worldwide licensing and development agreement for BEMA® Buprenorphine with Endo. Under terms of the agreement, Endo will be responsible for the manufacturing, distribution, marketing and sales of BEMA® Buprenorphine on a worldwide basis. Endo will commercialize BEMA® Buprenorphine outside the U.S. through its own efforts or through regional partnerships. Both companies will collaborate on the planning and finalization of the Phase 3 clinical development program and regulatory strategy for BEMA® Buprenorphine for chronic pain. We will maintain responsibility for the conduct of planned clinical studies leading up to the submission of the New Drug Application (NDA). Endo will have the responsibility of submitting the NDA and managing the interactions with the FDA. We plan to initiate two Phase 3 clinical studies, one in opioid naïve and one in opioid experienced patients by the middle of 2012.

BEMA® Buprenorphine is intended to meet the need for a new narcotic and could be used for chronic pain, including lower back, osteoarthritis and rheumatoid arthritis. Compared to currently marketed products and products under development, we believe that BEMA® Buprenorphine 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;

7

Table of Contents

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 nonsteroidal 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 BEMA® Buprenorphine 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. According to Wolters Kluwer, the U.S. opioid market exceeded $10 billion in sales in 2011. Due to the ability of BEMA® Buprenorphine to potentially participate in the chronic pain market, we estimate that BEMA® Buprenorphine (low dose) has the potential to exceed $500 million in annual peak sales.

BEMA® Buprenorphine/Naloxone (opioid dependence)

We are also investigating a higher dose formulation of BEMA® Buprenorphine combined with the abuse deterrent naloxone for the treatment of opioid dependence. Because of its lower propensity for abuse and addiction, BEMA® Buprenorphine (high dose) may also serve as a treatment for opioid dependence by preventing opioid addicted patients withdrawal symptoms while simultaneously maintaining pain control. Currently in the U.S. there are two buprenorphine products approved for this indication with 2011 total retail sales in excess of $1.4 billion. We believe BEMA® Buprenorphine/Naloxone has the potential to offer advantages over these products. We estimate that BEMA® Buprenorphine for the treatment of opioid dependence has the potential to achieve over $250 million in annual peak sales. We expect to finalize our formulation and complete a pivotal bioequivalence study in 2012 to support a possible NDA filing in the first half of 2013.

BEMA® Granisetron

This product candidate utilizes the BEMA® technology to deliver the 5-HT3 receptor antagonist Granisetron (marketed as Kytril®), an FDA approved antiemetic to prevent the nausea and vomiting often encountered following cancer chemotherapy and radiation. According to retail sales data from Wolters Kluwer, the U.S. market for 5-HT3 antagonists exceeds $2 billion. We filed an Investigational New Drug (IND) application for BEMA® Granisetron in early 2011. We believe that, in the presence of nausea and vomiting, BEMA® Granisetron would have the potential for better tolerance than oral formulations, as well as potential for better and more consistent absorption.