BIODELIVERY SCIENCES INTERNATIONAL INC
Form 10-K
March 16, 2017
Table of Contents

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

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

For the fiscal year ended December 31, 2016

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)**

Registrant 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

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

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 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 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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes No

The aggregate market value of the voting and non-voting common equity held by non-affiliates as of June 30, 2016 was approximately $93,505,279 based on the closing sale price of the company s common stock on such date of $2.36 per share, as reported by the NASDAQ Capital Market.

As of March 14, 2017, there were 54,812,113 shares of company common stock issued and 54,796,622 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, 2016

TABLE OF CONTENTS

Cautionary Note on Forward-Looking Statements		1
PART I		2
Item 1.	Description of Business	2
Item 1A.	Risk Factors	27
Item 1B.	Unresolved Staff Comments	45
Item 2.	Description of Property	45
Item 3.	Legal Proceedings	46
Item 4.	Mine Safety Disclosure	49
PART II		50
Item 5.	Market for Common Equity and Related Stockholder Matters	50
Item 6.	Selected Financial Data	51
Item 7.	Management_s Discussion and Analysis of Financial Condition and Results of Operations	52
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	69
Item 8.	Financial Statements	70
Item 9.	Changes In and Disagreements with Accountants on Accounting and Financial Disclosure	70
Item 9A.	Controls and Procedures	70
Item 9B.	Other Information	71
PART III		72
Item 10.	Directors, Executive Officers and Corporate Governance	72
Item 11.	Executive Compensation	87
Item 12	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	95
Item 13.	Certain Relationships and Related Transactions, and Director Independence	97
Item 14.	Principal Accountant Fees and Services	97
PART IV		99
Item 15.	Exhibits, Financial Statement Schedules	99
Item 16.	Form 10-K Summary	101

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.

Table of Contents

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® and BELBUCA® which 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, inter partes reexaminations and PIV litigations) or other claims or disputes relating to our business, technologies, patents, 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.

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 partnership 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 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 products BUNAVAIL® (buprenorphine and naloxone) buccal film and BELBUCA® (buprenorphine) buccal film, 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. 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 is set out below:

BELBUCA® (buprenorphine) buccal film for Chronic Pain

BELBUCA® is a partial mu-opioid agonist and a treatment indicated 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 former commercial partner, Endo Pharmaceuticals Inc. (or Endo), received approval of the New Drug Application (or NDA) for BELBUCA® on October 23, 2015.

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 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 included: (i) a $30 million upfront, non-refundable license fee, which we received in January 2012; (ii) $95 million in milestone payments based on achievement of pre-defined intellectual property, clinical development and regulatory events (which we have received following receipt of a $50 million milestone payment associated with the FDA approval of BELBUCA®); (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.

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 amount of $15 million in May 2012, and also related to the issuance of the patent, received an additional milestone payment of $20 million paid at the time of approval of the NDA by the FDA for BELBUCA® for the treatment of chronic pain, resulting in a total milestone payment at FDA approval of $50 million. Such amounts are included in the aforementioned $95 million in potential milestone payments based on intellectual property and clinical development and regulatory events. The aforementioned $20 million patent-related payment had been deferred for future revenue recognition and was to be earned over the extended patent period from 2020 to 2027. This $20 million will now be recognized as revenue in January 2017. (See below for Endo Termination).

Table of Contents

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).

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=0.0012) 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 during the double blind portion of the study were nausea (10% vs. 7%, respectively), vomiting (4% vs. <1%, respectively) and constipation (4% vs. 3%, 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<0.00001) 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% vs. 7%, respectively), vomiting (5% vs. 2%, respectively) and constipation (3% vs. 1%, 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 in 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 triggered and we received an additional $10 million milestone payment from Endo.

On October 26, 2015, we and Endo announced the FDA approval of BELBUCA® for use in patients with chronic pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The approval of BELBUCA® was based on the two double-blind, placebo-controlled, enriched-enrollment Phase 3 studies. A total of 1,559 opioid experienced (study BUP-307) and opioid naïve (BUP-308) patients received study drug. In both studies, BELBUCA® demonstrated a consistent, statistically significant improvement in patient-reported pain relief at every week from baseline to week 12, compared to placebo. BELBUCA® is available in seven dose strengths, allowing for flexible dosing ranging from 75 mcg to 900 mcg every 12 hours. This enables physicians to individualize titration and treatment based on the optimally effective and tolerable dose for each patient. The FDA s approval of BELBUCA® triggered a milestone payment to us from Endo of $50 million, of which $20 million had been deferred for future revenue recognition. (See below for Endo Termination).

BELBUCA® became commercially available from Endo in February 2016. Endo reported favorable early healthcare provider feedback and positive patient experience with regard to efficacy, tolerability and the buccal film formulation. Endo also filed a submission for BELBUCA® with Health Canada in the second quarter of 2016.

On December 8, 2016, we announced an agreement with Endo terminating Endo s licensing of rights for BELBUCA®. This announcement followed a strategic decision made by Endo to discontinue commercial efforts of its branded pain business. On January 6, 2017, we announced the closing of the transaction to reacquire the license to BELBUCA® from Endo. As a result, the worldwide rights to BELBUCA® were transferred back to us. Going forward, we will not be responsible for future royalties or milestone payments to Endo, and Endo will not be obligated to any future milestone payments to us.

Behind a revised commercialized plan based on market research conducted primarily by Endo that took into consideration the current climate for prescribing opioids for chronic pain, as such we are initially leveraging our existing sales force to capitalize on commercial synergies with BUNAVAIL for a focused commercial approach targeting identified healthcare providers which we believe creates the potential to incrementally grow BELBUCA® sales without the requirement of significant resources. We will also explore other options for longer-term growth for BELBUCA®. In mid-January 2017, we completed the expansion and training of our sales force, allowing for promotion of BELBUCA® to commence in late January. BELBUCA® and BUNAVAIL® (described below) are supported by a field force of sixty-five sales representatives and five regional sales managers.

Table of Contents

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 important 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, exceeded $2.2 billion in sales in the U.S in 2016.

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 and 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% 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.

On November 3, 2014, we announced the availability of BUNAVAIL® in the U.S. During the year ended 2015, we recognized $4.2 million in BUNAVAIL® sales revenue in its first full year on the market. In 2016, we took several steps to grow sales and profitability of the product including consolidating the sales force to focus on our most productive territories and executing additional managed care contracts. Six such agreements were secured between July and November 2016. BUNAVAIL® sales in 2016 were $8.3 million, representing a 98% increase from the previous year.

As a result of the reacquisition of BELBUCA® in January 2017, our field sales force is focused primarily on BELBUCA®, with BUNAVAIL® efforts limited to current BUNAVAIL® prescribers and on increasing prescriptions related to current, upcoming and future managed care contracts where BUNAVAIL is placed in a favorable position.

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.

Table of Contents

In 2010, we licensed 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 is marketed as PAINKYL . The Kunwha License Agreement was terminated on August 31, 2015.

Although we have generated licensing-related and other revenue to date from the commercial sales of ONSOLIS®/BREAKYL /PAINKYL , 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 was launched on a country by country basis starting in the fourth quarter of 2012 and continues to be sold by Meda. TTY launched PAINKYL in Taiwan in 2015.

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.

On March 12, 2012, we announced the postponement of the U.S. relaunch 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, were raised by the FDA during an inspection of our North American manufacturing partner for ONSOLIS®, Aveva Drug Delivery Systems, Inc. (or Aveva) which is now a subsidiary of Apotex (or Apotex). While the appearance issues did not affect the product s underlying integrity, safety or performance, the FDA believed 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 submitted a prior approval supplement that responded to FDA questions and led to FDA approval of the new formulation of ONSOLIS® in August 2015.

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.

On May 11, 2016, we announced the signing of a licensing agreement under which we granted to Collegium Pharmaceutical, Inc. (or Collegium) the exclusive rights to develop and commercialize ONSOLIS® in the U.S. Under terms of the agreement, Collegium will be responsible for the manufacturing, distribution, marketing and sales of ONSOLIS® in the U.S. Both companies are collaborating on the ongoing transfer of manufacturing, which includes submission of a Prior Approval Supplement (Supplement) to the U.S. Food and Drug Administration (FDA). Upon approval of the Supplement, the New Drug Application (NDA) and manufacturing responsibility will be transferred to Collegium. Financial terms of our agreement with Collegium include a $2.5 million upfront non-refundable payment, a $4 million payment upon first commercial sale, $3 million payable to us related to ONSOLIS® patent milestone, up to $17 million in potential payments based on achievement of performance and sales milestones, and upper-teen

percent royalties based on various annual U.S. net sales thresholds. Meda shares in a major portion of the proceeds of our partnership with Collegium, and the completion of this transaction with Collegium required the execution of a definitive termination agreement between us and Meda embodying those royalty-sharing terms and certain other provisions. Meda continues to commercialize ONSOLIS® under the brand name BREAKYL in the E.U.

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 Therapeutics (or Arcion), under which we would 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.

Table of Contents

In March 2015, we announced that the primary efficacy endpoint in a Phase 3 study of Clonidine Topical Gel compared to placebo did not meet statistical significance, although certain secondary endpoints showed statistically significant improvement over placebo. Final analysis of the study identified a sizeable patient population with a statistically significant improvement (n=158; p<0.02) in pain score vs placebo. Following thorough analysis of the data and identification of the reasons behind the study results, we announced on December 8, 2015 that we had initiated a Phase 2b study. On December 13, 2016, we announced that the Phase 2b study failed to show a statistically significant difference in pain relief between Clonidine Topical Gel and placebo, and as a result we have no further plans for development of Clonidine Topical Gel. Given the perceived lack of efficacy, at least in this dosage form and at this strength, and given the resources to support the product by us, the rights to Clonidine Topical Gel were returned to Arcion in February 2017.

Buprenorphine Depot Injection

In 2014, we entered into an exclusive agreement with Evonik Corporation (or 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).

In 2015, we completed initial development work and preclinical studies which have resulted in the identification of a formulation we believe is capable of providing 30 days of continuous buprenorphine treatment. During a pre-IND meeting with FDA in November 2015, FDA requested an additional study to assess the fate of the polymers used in the formulation. In 2016, we completed this study as well as additional preclinical work and other activities to support a planned Phase 1 clinical study. We submitted an Investigational New Drug application (or IND) for this product candidate to FDA in December 2016.

Additional Overview Information

From our inception through December 31, 2016, we have recorded accumulated losses totaling approximately $310.3 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 or other products or product candidates that we may acquire or in-license in the future, 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 BELBUCA® and BUNAVAIL®;

partnering with other pharmaceutical companies, as we have done with Collegium and Meda, to assist in the distribution and commercialization of our products, for which we would expect to receive an upfront payment, milestones and royalty payments; and

securing proceeds from public and private financings and other potential 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®, BELBUCA®, ONSOLIS®, 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

Table of Contents

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;
- permit absorption without patients being required to move the product around in the mouth for absorption, thus avoiding patient intervariability;
- allow for unidirectional drug flow into the mucosa as a result of a backing layer on the side of the BEMA® film facing into the patient s mouth
- 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 and naloxone) buccal film and again in 2015 with the approval of BELBUCA® (buprenorphine) 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:

single and multiple dose toxicity studies in a single animal species,

pharmacokinetic evaluation of the new dosage form in humans,

stability data on the drug substance,

description of drug product components and formulation,

description and validation of manufacturing processes,

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.

Table of Contents

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 markets with unmet needs and new dosage forms of known drugs. 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®, and BUNAVAIL® 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® and its Termination

On January 6, 2012, we entered into the world-wide licensing and development agreement for BELBUCA® with Endo, which was subsequently terminated as described above. Under terms of the agreement, Endo was responsible for the manufacturing, distribution, marketing and sales of BELBUCA® on a worldwide basis. The agreement called for Endo to commercialize BELBUCA® outside the U.S. through its own efforts or through regional partnerships. In the U.S., we and Endo collaborated on the planning and finalization of the Phase 3 clinical development program and regulatory strategy for BELBUCA® for chronic pain. On October 23, 2015 the FDA approved BELBUCA® for licensing in the United States.

In aggregate, the agreement was 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. We would have received 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 also received an additional milestone payment of $20 million which was paid at the time of approval of a NDA by the FDA for BELBUCA®. The aforementioned $20 million patent-related payment will be earned over the extended patent period from 2020 to 2027. As mentioned above, the obligations of this milestone were extinguished upon the closing of the termination arrangements. 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 triggered a $10 million milestone payment due from Endo to us. As stated above, on October 23, 2015 the FDA approved BELBUCA® for licensing in the United States, which we announced on October 26, 2015. The FDA s approval of BELBUCA® triggered a milestone payment to us from Endo of $50 million, of which $20 million has been deferred for future revenue recognition as the payment is contingently refundable in the event a generic product is commercially launched during the patent extension period. As mentioned below, the obligations of this milestone were extinguished upon the closing of the termination agreement. This $20 million will now be recognized as revenue in January 2017.

On December 8, 2016 we announced we had entered into a termination agreement with Endo (the Endo Termination Agreement) terminating Endo s licensing of rights for BELBUCA® CIII (buprenorphine) buccal film. The transaction terminating Endo s licensing of rights for BELBUCA® closed on January 6, 2017. This transaction follows a strategic decision announced by Endo in December regarding its U.S. branded pain business. As a result of the agreement, the world-wide rights to BELBUCA® were transferred back to us. We are not responsible for future royalties or milestone payments to Endo and Endo will not be obligated to any future milestone payments to us. The termination agreement with Endo is filed as an exhibit to this Report.

At the closing of the transactions contemplated by the Endo Termination Agreement we purchased from Endo the following assets (which we refer to as the Assets): (i) current BELBUCA® product inventory and work-in-progress, (ii) material manufacturing contracts related to BELBUCA®, (iii) BELBUCA-related domain names and trademarks (including the BELBUCA® trademark), (iv) BELBUCA®-related manufacturing equipment, and (v) all pre-approval regulatory submissions, including any Investigational New Drug Applications and New Drug Applications, regulatory approvals and post-approval regulatory submissions concerning BELBUCA®. The purchase price for the Assets (which we refer to as the Asset Purchase Price) was equal to the sum of: (i) the aggregate book value of the portion of the transferred product inventory forecasted to be used or sold by the Company, (ii) the aggregate book value of work-in-progress inventory, and (iii) the assumption of any assumed liabilities. Upon Closing, we accepted transfer of the Assets and assumed and agreed to discharge when due all applicable liabilities assumed by us, which consisted of post-closing obligations for liabilities and payments associated with the Assets, the assumed contracts related to the Assets and applicable

Table of Contents

taxes (with the obligation for pre-closing and other certain liabilities resulting from the acts or omissions of Endo being retained by Endo).

The Asset Purchase Price, together with all other payments (including a non-compete covenant payment) due to Endo under the Endo Termination Agreement, will be paid to Endo in cash, in four quarterly installments on the last calendar day of each quarter in 2017. We are currently evaluating the financial impact of the Termination Agreement in accordance with US GAAP. Furthermore, we will not be responsible for future royalties or milestone payments to Endo, and Endo will not be obligated to any future milestone payments to us. The Termination Agreement contains customary representations and warranties and mutual releases and indemnification.

At the closing of the Termination Agreement, we and Endo entered into a Transition Services Agreement which will govern the post-closing rights and responsibilities of us and Endo in connection with the license termination and the transfer of the Assets to us. Under this agreement, we and Endo agreed to the handling of transition matters such as managing customer contracts, BELBUCA® price reporting, payments, returns and rebates, and customer and managed care relations. In connection therewith, Endo agreed to provide to us an agreed upon number of work hours to be provided by Endo personnel during the transition for certain of these transition services and other assistance with respect to the transition of BELBUCA® to us.

In conjunction with the aforementioned Endo Termination Agreement, on December 7, 2016, we also entered into a distribution agreement (which we refer to as the Distribution Agreement) with Par Pharmaceuticals, Inc. (or Par) for the distribution of an authorized generic BELBUCA® product after the launch of a generic BELBUCA® product by a third party. The Distribution Agreement covers distribution within the entire United States, has an initial term of three years after the launch of a generic BELBUCA® product by a third party, an initial automatic renewal period of two years, and additional automatic one-year renewal periods thereafter, which will occur unless either party provides written notice of termination an agreed upon period of time prior to the expiration of the initial term or any renewal term. In exchange for distribution rights of the generic product, Par will pay us an agreed upon base purchase price and a deferred purchase price equal to a percentage of profit (as such term is specifically agreed to in the Distribution Agreement) with respect to units of each dosage strength of generic product. During the term of the Distribution Agreement, Par is precluded from manufacturing for sale in the United States, or distributing in the United States, any equivalent product, provided that nothing prohibits Par from continuing or undertaking to develop any equivalent product or selling such equivalent product outside of the U.S. The Distribution Agreement contains customary termination provisions for bankruptcy, withdrawal of product from the market, and regulatory and legislative changes, as well as a termination right for insufficient profits or Par s acquisition by or of a party challenging our patents with respect to BELBUCA®.

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.

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).

Table of Contents

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 South 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.

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 authorization for ONSOLIS® in the U.S. and the right to seek marketing authorizations for ONSOLIS® in Canada and Mexico. Following the return of the U.S. marketing authorization from Meda, we submitted a prior approval supplement for the new formulation to the FDA in March 2015, which was approved in August 2016. In connection with the return of the U.S. marketing authorization by Meda to us in January 2015, the remaining U.S.-related deferred revenue of $1.0 million was recorded as contract revenue during the year ended December 31, 2015. There was no remaining U.S.-related contract revenue to record during the year ended December 31, 2016. On February 27, 2016, we entered into an extension of the assignment and revenue sharing agreement to extend the period until December 31, 2016.

Efforts to extend our supply agreement with its ONSOLIS® manufacturer, Aveva, which is now a subsidiary of Apotex, Inc., were unsuccessful and the agreement expired. However, we identified an alternate supplier and requested guidance from the FDA on the specific requirements for obtaining approval to supply product from this new vendor. Based on current estimates, we expect to submit the necessary documentation to the FDA for qualification of the new manufacturer by mid-2017.

Collegium License and Development Agreement for ONSOLIS®

On May 11, 2016, we entered into a definitive License and Development Agreement (which we refer to as the Collegium Agreement) with Collegium Pharmaceutical, Inc. (or Collegium) under which we granted Collegium the exclusive rights to develop and commercialize ONSOLIS® in the U.S. Under the terms of the Collegium Agreement, Collegium will be responsible for the manufacturing, distribution, marketing and sales of ONSOLIS® in the U.S. We are obligated to use commercially reasonable efforts to continue the transfer of manufacturing to the anticipated manufacturer for ONSOLIS® and to submit a corresponding Prior Approval Supplement (the Supplement) to the FDA with respect to the current NDA for ONSOLIS®. Following approval of the Supplement, the NDA and manufacturing responsibility for ONSOLIS® (including the manufacturing relationship with our manufacturer, subject to our entering into an appropriate agreement with such manufacturer that is acceptable and assignable to Collegium) will be transferred to Collegium.

Financial terms of the License Agreement include;

- $2.5 million upfront non-refundable payment, (received in June 2016);

- reimbursement to us for a pre-determined amount of the remaining expenses associated with the ongoing transfer of the manufacturing of ONSOLIS®;

$4 million payable to us upon first commercial sale of ONSOLIS® in the U.S;

$3 million payable to us related to ONSOLIS® patent milestone;

up to $17 million in potential payments to us based on achievement of certain performance and sales milestones; and

upper-teen percent royalties payable by Collegium to us based on various annual U.S. net sales thresholds, subject to customary adjustments and the royalty sharing arrangements described below.

The Collegium Agreement also contains customary termination provisions that include a right by either party to terminate upon the other party s uncured material breach, insolvency or bankruptcy, as well as in the event a certain commercial milestone is not met.

ONSOLIS® was originally licensed to, and launched