BIODELIVERY SCIENCES INTERNATIONAL INC
Form S-3
July 02, 2015
Table of Contents

As filed with the Securities and Exchange Commission on July 2, 2015

Registration No. 333-

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

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 Number)**

4131 ParkLake Avenue, Suite #225

Raleigh, NC 27612

(919) 582-9050

(Address, including zip code, and telephone number, including area code, of registrant s principal executive offices)

Mark A. Sirgo, Pharm.D.

4131 ParkLake Avenue, Suite # 225

Raleigh, NC 27612

(919) 582-9050

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Barry I. Grossman, Esq.

Lawrence A. Rosenbloom, Esq.

Ellenoff Grossman & Schole LLP

1345 Avenue of Americas

New York, New York 10105

(212) 370-1300

Fax: (212) 370-7889

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box: ¨

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box: x

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering: ¨

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. ¨

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. ¨

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

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Aggregate Offering Price per Security(1)	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee(1)(2)
Common Stock, par value $.001 per share(3)				
Preferred Stock, par value $.001 per share(4)				
Debt Securities				
Warrants(5)				
Rights(6)				
Units(7)				
TOTAL	$150,000,000(8)		$150,000,000	$17,430.00(9)

(1) Pursuant to General Instruction II.D to Form S-3, the Amount to be Registered, Proposed Maximum Aggregate Offering Price per Security and Proposed Maximum Aggregate Offering Price have been omitted for each class of securities that are registered hereby.

(2) The registration fee for the unallocated securities registered hereby has been calculated in accordance with Rule 457(o) under the Securities Act of 1933, as amended, and reflects the maximum offering price of securities that may be issued rather than the principal amount of any securities that may be issued at a discount.

(3) An indeterminate number of shares of common stock of BioDelivery Sciences International, Inc. are covered by this Registration Statement.

(4) An indeterminate number of shares of preferred stock of BioDelivery Sciences International, Inc. are covered by this Registration Statement. Shares of common stock issued upon conversion of the debt securities and the preferred stock will be issued without the payment of additional consideration.

(5) An indeterminate number of warrants of BioDelivery Sciences International, Inc., each representing the right to purchase an indeterminate number of shares of preferred stock or shares of common stock or amount of debt securities, each of which are registered hereby, are covered by this Registration Statement.

(6) Rights evidencing rights to purchase securities of BioDelivery Sciences International, Inc.

(7) Each Unit consists of any combination of two or more of the securities being registered hereby.

(8) Also registered hereby are such additional and indeterminable number of securities as may be issuable due to adjustments for changes resulting from stock dividends, stock splits and similar changes as well as anti-dilution provisions applicable to the warrants.

(9) The registration fee has been calculated in accordance with Regulation 457(o) under the Securities Act of 1933, as amended, based on the current statutory fee of $116.20 per million.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until this Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

Table of Contents

EXPLANATORY NOTE

This registration statement contains two prospectuses:

- a base prospectus which covers the offering, issuance and sale by us of up to $150,000,000 of our common stock, preferred stock, debt securities, warrants, rights and/or units; and

- a sales agreement prospectus covering the offering, issuance and sale by the Registrant of up to $40,000,000 of our common stock that may be issued and sold under a sales agreement with Cantor Fitzgerald & Co.

The base prospectus immediately follows this explanatory note. The sales agreement prospectus immediately follows the base prospectus. The $40,000,000 of common stock that may be offered, issued and sold by us under the sales agreement prospectus is included in the $150,000,000 of securities that may be offered, issued and sold by us under the base prospectus. The sales agreement prospectus includes the base prospectus, except that the sales agreement prospectus contains a different front and back cover page, and sets forth additional information in the sections titled About this Prospectus, The Offering, Risk Factors, Use of Proceeds, Dilution, Plan of Distribution and Legal Matters. The cover such additional information contained in the sales agreement prospectus are set forth in the pages following the base prospectus included herein.

Table of Contents

The information in this prospectus is not complete and may be changed. We may not sell the securities until the Registration Statement filed with the Securities and Exchange Commission, of which this prospectus is a part, is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JULY 2, 2015

PROSPECTUS

$150,000,000

Common Stock
Preferred Stock
Debt Securities
Warrants
Rights
Units

We may offer and sell from time to time, in one or more series, any one of the following securities of our company, for total gross proceeds up to $150,000,000:

common stock;

preferred stock;

secured or unsecured debt securities consisting of notes, debentures or other evidences of indebtedness which may be senior debt securities, senior subordinated debt securities or subordinated debt securities, each of which may be convertible into equity securities;

warrants to purchase our securities;

rights to purchase any of the foregoing securities; or

units comprised of, or other combinations of, the foregoing securities.

We will provide specific terms of these offerings and securities in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement, and any documents incorporated by reference, may also add, update or change information contained in this prospectus. You should read this prospectus, the applicable prospectus supplement, any documents incorporated by reference and any related free writing prospectus carefully before buying any of the securities being offered.

We may offer and sell these securities to or through one or more underwriters, dealers and agents, or directly to purchasers, on a continuous or delayed basis.

Our common stock is traded on The NASDAQ Capital Market under the symbol BDSI. The last reported sale price of our common stock on The NASDAQ Capital Market on June 30, 2015 was $7.96 per share.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading Risk Factors contained in the applicable prospectus supplement and in any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus or any prospectus supplement before making a decision to purchase our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 2015.

Table of Contents

TABLE OF CONTENTS

You should rely only on the information we have provided or incorporated by reference in this prospectus or in any prospectus supplement. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus or in any prospectus supplement.

This prospectus and any prospectus supplement is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so.

You should assume that the information contained in this prospectus and in any prospectus supplement is accurate only as of their respective dates and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any prospective supplement or any sale of securities.

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a shelf registration process. Under this shelf registration process, we may offer and sell, either individually or in combination, in one or more offerings, any combination of the securities described in this prospectus, for total gross proceeds of up to $150,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents that we have incorporated by reference into this prospectus.

We urge you to read carefully this prospectus, any applicable prospectus supplement and any free writing prospectuses we have authorized for use in connection with a specific offering, together with the information incorporated herein by reference as described under the heading Incorporation of Certain Information by Reference, before investing in any of the securities being offered. You should rely only on the information contained in, or incorporated by reference into, this prospectus and any applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We have not authorized anyone to provide you with different or additional information. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so.

The information appearing in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the section entitled Where You Can Find More Information.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Table of Contents

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement and the documents we have filed or will file with the SEC that are or will be incorporated by reference into this prospectus and the accompanying prospectus supplement contain forward-looking statements, within the meaning of Section 27A of the Securities Act of 1933, as amended (which we refer to as the Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (which we refer to as the Exchange Act), that involve significant risks and uncertainties. Any statements contained, or incorporated by reference, in this prospectus and any accompanying prospectus that are not statements of historical fact may be forward-looking statements. When we use the words anticipate, believe, could, estimate, expect, intend, may, plan, predict, pro 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 our research, development, commercialization, manufacturing, marketing and distribution efforts relating to our BEMA® 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 (iii) 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 BUNAVAIL®, which is the first product we are self-commercializing;
- our ability to generate commercially viable products and the market acceptance of our BEMA® technology platform and our proposed products and product candidates;
- our ability to finance our operations on acceptable terms, either through the raising of capital, the incurrence of convertible or other indebtedness or through strategic financing or commercialization partnerships;
- our expectations about the potential market sizes and market participation potential for our approved or proposed products;
- the protection and control afforded by our patents or other intellectual property, and any interest patents or other intellectual property that we license, 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 (and related activities, including inter-partes reviews and inter-partes reexaminations) or other claims or disputes relating to our business, technologies, products or processes;

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

Table of Contents

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; and

The foregoing does not represent an exhaustive list of risks that may impact upon the forward-looking statements used herein or in the documents incorporated by reference herein. Please see Risk Factors in our reports filed with the SEC or in a prospectus supplement related to this prospectus 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 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 prospectus and any accompanying prospectus supplement are based on information available to us on the date hereof or thereof. 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 (or incorporated by reference in) this prospectus, any accompanying prospectus and the documents we have filed with the SEC.

Table of Contents

PROSPECTUS SUMMARY

The following summary highlights selected information contained or incorporated by reference in this prospectus. This summary does not contain all of the information you should consider before investing in the securities. Before making an investment decision, you should read the entire prospectus and any supplement hereto carefully, including the risk factors section as well as the financial statements and the notes to the financial statements incorporated herein by reference.

In this prospectus and any amendment or supplement hereto, unless otherwise indicated, the terms BioDelivery Sciences International, Inc., BDSI, the Company, we, us, and our refer and relate to BioDelivery Sciences International, Inc. and its consolidated subsidiaries.

Overview

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

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

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

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

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

BELBUCA (BEMA® Buprenorphine) for Chronic Pain

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

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

Table of Contents

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

One of the key intellectual property milestones under our Endo Agreement was achieved in February 2012, when the U.S. Patent and Trademark Office (or USPTO) issued a Notice of Allowance regarding one of our patent applications (No. 13/184306) which, once the patent was granted in April 2012, extended the exclusivity of the BEMA® drug delivery technology for BELBUCA (as well as BUNAVAIL®, as discussed below) from 2020 to 2027. As a result, we received a milestone payment from Endo in the amount of $15 million in May 2012, and also related to the issuance of the patent, will receive an additional milestone payment of $20 million at the time of approval of a New Drug Application (or NDA) by the FDA for BELBUCA for the treatment of chronic pain. Such amounts are included in the aforementioned $95 million in potential milestone payments based on intellectual property and clinical development and regulatory events.

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

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

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

On July 7, 2014, we announced with Endo positive top-line results from the Phase 3 efficacy study of BELBUCA in opioid- experienced subjects. The trial successfully met its primary efficacy endpoint in demonstrating that BELBUCA resulted in significantly ($p<0.0001$) improved chronic pain relief compared to placebo. Additional secondary endpoints were supportive of the efficacy of BELBUCA compared to placebo. The

Table of Contents

most commonly reported adverse events in patients treated with BELBUCA compared to placebo were nausea (7.5% vs. 7.4%, respectively) and vomiting (5.5% vs. 2.3%, respectively). Locking of the database for the opioid experienced study triggered an additional $10 million milestone payment from Endo per the terms of the license agreement, which we received July 2014.

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

BUNAVAIL® (buprenorphine and naloxone) buccal film

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

In September 2012, we announced the positive outcome of the pivotal pharmacokinetic study comparing BUNAVAIL® to Suboxone ® sublingual tablets. The study was designed to compare the relative bioavailability of buprenorphine and naloxone between BUNAVAIL ® and the reference product, Suboxone ® tablets. The results demonstrated that the two key pharmacokinetic parameters, maximum drug plasma concentration (Cmax) and total drug exposure (AUC), for buprenorphine were comparable to Suboxone ® sublingual tablet, and that the same parameters for naloxone were similar or less than Suboxone ® tablet. This was followed by initiation of the safety study requested by FDA, assessing the safety and tolerability of BUNAVAIL ® in patients converted from a stable dose of Suboxone ® (buprenorphine/naloxone) sublingual tablets or films. A total of 249 patients were enrolled in the study, (191 patients completed) which completed in December 2012. Results of the study showed a very favorable safety and tolerability profile along with strong study subject retention and high dose form acceptability ratings. Data showed that over 91% of patients who switched from Suboxone ® film or tablets considered the taste of BUNAVAIL ® to be very pleasant, pleasant or neutral and over 82% rated the ease of use of BUNAVAIL® as very easy, easy or neutral. The study also showed a decrease in the incidence of constipation symptoms from 41% at baseline, before conversion of patients from Suboxone tablets or films to BUNAVAIL ®, to 13% following 12 weeks of treatment with BUNAVAIL ®.

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

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

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

Table of Contents

ONSOLIS® (fentanyl buccal soluble film)

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

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

We granted commercialization and distribution rights for ONSOLIS® on a worldwide basis (except in South Korea and Taiwan) to Meda. Meda s U.S. subsidiary, Meda Pharmaceuticals, based in Somerset, New Jersey, is a specialty pharmaceutical company that develops, markets and sells branded prescription therapeutics. Meda secured access to additional markets through acquisition of European businesses from Valeant Pharmaceuticals International, Inc., which we refer to herein as Valeant and a joint venture with Valeant covering Australia, Mexico and Canada. In 2010, we secured commercialization rights for ONSOLIS® for the remaining worldwide territories through execution of licensing agreements with KUNWHA Pharmaceutical Co., Ltd. (or Kunwha), for South Korea and TTY Biopharm Co., Ltd. (or TTY) for Taiwan where the product will be marketed as PAINKYL .

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

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

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

Table of Contents

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

Clonidine Topical Gel

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

We believe that the PDN market is highly under-served by existing products and therefore there is a strong scientific rationale for developing a topical treatment for PDN that delivers analgesia in a way that avoids systemic side effects. Evidence has shown that clonidine stimulates an inhibitory receptor in the skin associated with pain fibers. Arcion has assessed its effectiveness in reducing pain in PDN in a double-blind, placebo-controlled, Phase 2 study where the primary study endpoint was the change in pain intensity over a 3 month treatment period in diabetic foot pain. A significant treatment difference was seen in the planned subset analysis of diabetic patients who had documented evidence of functioning pain receptors in the skin of the lower leg (p=0.01, n=63) thus, at a minimum, supporting the effectiveness of topical clonidine in diabetic patients with functioning pain receptors of the skin. In the overall population that included patients without functioning nerve receptors , there was a trend favoring topical Clonidine Topical Gel (p=0.07, n= 182), though the overall results did not reach statistical significance. Oral medications that are approved for the treatment of PDN include anticonvulsants such as Lyrica (pregabalin), the antidepressant Cymbalta ® (duloxetine) and the opioid Nucynta ® ER (tapentadol ER), with sales for the treatment of neuropathic pain totaling over $3 billion in the U.S. according to Datamonitor. These treatments are modestly effective in relieving symptoms and their use can be limited by adverse effects and drug interactions.

In late March 2015, we announced that the primary efficacy endpoint in our Phase 3 clinical study of Clonidine Topical Gel for PDN compared to placebo for the treatment of PDN did not meet statistical significance. Certain secondary endpoints showed statistically significant improvement over the placebo. In addition, a strong safety profile for the product was observed. Based on our ongoing analysis, we believe that the data from this study supports continued development of this product. Our analysis showed an unusually high placebo response in the cohort of patients that entered the trial following our previously announced interim analysis of the study. Generally speaking, we believe there may be study design features that might be able to mitigate this response in all patients that would enter a subsequent study of Clonidine Topical Gel, and we are presently considering these features as we evaluate the potential for additional study of this product candidate. We are therefore currently in the process of determining what the next steps in the development pathway should be and whether our decision may require FDA consultation. One possibility is that we would do a small scale study that takes into account the design features that we believe could mitigate the placebo response we saw in our initial Phase 3 trial. If we decide to pursue this type of study or any next study, it would not likely occur before fourth quarter of 2015.

Buprenorphine Depot Injection

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

Table of Contents

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

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

Additional Information

From our inception through March 31, 2015, we have recorded accumulated losses totaling approximately $213.7 million. Our historical operating losses have resulted principally from our research and development activities, including clinical trial activities for our product candidates and general and administrative expenses. Ultimately, if we secure additional approvals from the FDA and other regulatory bodies throughout the world for our product candidates, our goal will be to augment our current sources of revenue and, as applicable, deferred revenue (principally licensing fees), with sales of such products or royalties from such sales, on which we may pay royalties or other fees to our licensors and/or third-party collaborators as applicable.

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

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

We have based our estimates of development costs, market size estimates, peak annual sales projections and similar matters described below and elsewhere in this prospectus on our market research, third party reports and publicly available information which we consider reliable. However, readers are advised that the projected dates for filing and approval of our INDs or NDAs with the FDA or other regulatory authorities, our estimates of development costs, our projected sales and similar metrics regarding BUNAVAIL ® , ONSOLIS ® , BELBUCA , Clonidine Topical Gel, Buprenorphine Depot Injection or any other product candidates discussed below and elsewhere in this prospectus and any accompanying prospectus supplement are merely estimates and subject to many factors, many of which may be beyond our control, which will likely cause us to revise such estimates. Readers are also advised that our projected sales figures do not take into account the royalties and other payments we will need to make to our licensors and strategic partners. Our estimates are based upon our management s reasonable judgments given the information available and their previous experiences, although such estimates may not prove to be accurate.

The Securities We May Offer

We may offer and sell from time to time up to an aggregate of $150,000,000 of any of, or units comprised of, or other combinations of, the following securities:

Common Stock. We may issue shares of our common stock. Holders of common stock are entitled to receive ratably dividends if, as and when dividends are declared from time to time by our board of directors out of funds legally available for that purpose, after payment of dividends required to be paid on outstanding preferred stock or series common stock. Holders of common stock are entitled to one vote per share. Holders of common stock have no cumulative voting rights in the election of directors.

Table of Contents

Preferred Stock. We may issue shares of our preferred stock in one or more series. Our board of directors will determine the dividend, voting, conversion and other rights of the series of preferred stock being offered.

Debt Securities. We may offer debt securities, which may be secured or unsecured, senior, senior subordinated or subordinated, may be guaranteed by our subsidiaries, and may be convertible into shares of our common stock. We may issue debt securities either separately or together with, upon conversion of or in exchange for other securities. It is likely that the debt securities that we may issue will not be issued under an indenture.

Warrants. We may issue warrants to purchase shares of preferred stock, common stock or debt securities of our company. We may issue warrants independently or together with other securities. Warrants sold with other securities as a unit may be attached to or separate from the other securities. To the extent the warrants are publicly-traded, we will issue warrants under one or more warrant agreements between us and a warrant agent that we will name in the applicable prospectus supplement.

Rights. We may issue rights to purchase of preferred stock or common stock or debt securities of our company. We may issue rights independently or together with other securities. Rights sold with other securities as a unit may be attached to or separate from the other securities and may be (but shall not be required to be) publicly-listed securities.

Units. We may also issue units comprised of one or more of the other securities described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security.

Prospectus Supplement. We will describe the terms of any such offering in a supplement to this prospectus. Any prospectus supplement may also add, update or change information contained in this prospectus. Such prospectus supplement will contain, among other pertinent information, the following information about the offered securities:

- title and amount;
- offering price, underwriting discounts and commissions or agency fees, and our net proceeds;
- any market listing and trading symbol;
- names of lead or managing underwriters or agents and description of underwriting or agency arrangements; and
- the specific terms of the offered securities.

This prospectus may not be used to offer or sell securities without a prospectus supplement which includes a description of the method and terms of this offering.

Table of Contents

RISK FACTORS

We have included discussions of the risks, uncertainties and assumptions under the heading Risk Factors included in our Annual Report on Form 10-K for the year ended December 31, 2014, which risk factors are incorporated by reference into this prospectus. See Where You Can Find More Information for an explanation of how to get a copy of this report. Additional risks related to our securities may also be described in a prospectus supplement and in any related free writing prospectus that we may authorize to be provided to you.

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should carefully consider the risk factors we describe in any prospectus supplement and in any related free writing prospectus that we may authorize to be provided to you or in any report incorporated by reference into this prospectus or such prospectus supplement, including our Annual Report on Form 10-K for the year ended December 31, 2014, or any Annual Report on Form 10-K or Quarterly Report on Form 10-Q that is incorporated by reference into this prospectus or such prospectus supplement after the date of this prospectus. Although we discuss key risks in those risk factor descriptions, additional risks not currently known to us or that we currently deem immaterial also may impair our business. Our subsequent filings with the SEC may contain amended and updated discussions of significant risks. We cannot predict future risks or estimate the extent to which they may affect our financial performance.

Please also read carefully the section above entitled Cautionary Note Regarding Forward-Looking Statements.

RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth our ratio of fixed charges and preference dividends to earnings for each of the periods indicated. You should read this table in conjunction with the financial statements and notes incorporated by reference in this prospectus.

	For Fiscal Year Ended				
	December 31, 2014	December 31, 2013	December 31, 2012	December 31, 2011	December 31, 2010
Ratios of fixed charges and preference dividends to earnings	N/A	N/A	45.10	N/A	N/A

We have computed the ratio of fixed charges and preference dividends to earnings set forth above by dividing pre-tax loss before fixed charges and preference dividends by fixed charges and preference dividends. Fixed charges are the sum of the following:

- interest expensed and capitalized;
- amortized premiums related to indebtedness; and
- an estimate of the interest within rental expense.

We did not pay any cash dividends on any shares of our capital stock during the periods set forth above.

We did not record earnings for the fiscal years ended December 31, 2014, 2013, 2011 and 2010. Accordingly, our earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of fixed charges and preference dividends to earnings for such periods. The dollar amount of the deficiency in earnings available for fixed charges and preference dividends for the fiscal years ended December 31, 2014, 2013, 2011 and 2010 was approximately $54.2 million, $57.4 million, $23.3 million and $13.0 million, respectively.

Table of Contents

USE OF PROCEEDS

Except as otherwise disclosed in the applicable prospectus supplement, we intend to use the net proceeds from the sales of securities hereunder for the clinical and regulatory advancement of our product candidates; for commercialization of our products, including potential sales and marketing of products on our own behalf; to support of our partnered products; for potential acquisitions of new technologies and products or related companies, and to meet working capital needs. The amounts and timing of our use of the net proceeds from this offering will depend on a number of factors, such as the timing and progress of our research and development efforts, the timing and progress of any partnering and commercialization efforts, technological advances and the competitive environment for our products. As of the date of this prospectus, we cannot specify with certainty all of the particular uses for the net proceeds to us from the sale of the securities offered by us hereunder and the applicable prospectus supplement. Accordingly, our management will have broad discretion in the timing and application of these proceeds. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short-term, interest-bearing instruments.

DESCRIPTION OF CAPITAL STOCK AND SECURITIES WE MAY OFFER

General

The following description of our capital stock (which includes a description of securities we may offer pursuant to the registration statement of which this prospectus, as the same may be supplemented, forms a part) does not purport to be complete and is subject to and qualified in its entirety by our certificate of incorporation, as amended, and our amended and restated bylaws and by the applicable provisions of Delaware law.

Our authorized capital stock consists of 75,000,000 shares of common stock and 5,000,000 shares of preferred stock. As of the date of this prospectus, our outstanding capital stock consists of 52,421,435 shares of common stock, $.001 par value, and 2,093,155 shares of Series A Preferred Stock, par value $.001 per share. These figures do not include securities that may be issued: (i) pursuant to outstanding warrants to purchase shares of our common stock, (ii) pursuant to our Amended and Restated 2001 Incentive Plan or (iii) pursuant to our 2011 Equity Incentive Plan, as amended.

We, directly or through agents, dealers or underwriters designated from time to time, may offer, issue and sell, together or separately, up to $150,000,000 in the aggregate of:

- common stock;
- preferred stock;
- secured or unsecured debt securities consisting of notes, debentures or other evidences of indebtedness which may be senior debt securities, senior subordinated debt securities or subordinated debt securities, each of which may be convertible into equity securities;
- warrants to purchase our securities;
- rights to purchase our securities; or
- units comprised of, or other combinations of, the foregoing securities.

We may issue the debt securities as exchangeable for or convertible into shares of common stock, preferred stock or other securities. The preferred stock may also be exchangeable for and/or convertible into shares of common stock, another series of preferred stock or other securities. The debt securities, the preferred stock, the common stock and the warrants are collectively referred to in this prospectus as the securities. When a particular series of securities is offered, a supplement to this prospectus will be delivered with this prospectus, which will set

forth the terms of the offering and sale of the offered securities.

Table of Contents

Common Stock

As of the date of this prospectus, there were 52,436,926 shares of common stock issued and 52,421,435 shares of common stock outstanding, held of record by approximately 115 stockholders. The holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. Subject to preferential rights with respect to any outstanding preferred stock, holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of funds legally available therefore. In the event of our liquidation, dissolution or winding up, the holders of common stock are entitled to share ratably in all assets remaining after payment of liabilities and satisfaction of preferential rights of any outstanding preferred stock.

Our common stock has no preemptive or conversion rights or other subscription rights. There are no sinking fund provisions applicable to the common stock. The outstanding shares of common stock are fully paid and non-assessable.

Preferred Stock

Our certificate of incorporation, as amended, empowers our board of directors, without action by our shareholders, to issue up to 5,000,000 shares of preferred stock from time to time in one or more series, which preferred stock may be offered by this prospectus and supplements thereto. As of the date of this prospectus, we had 2,709,300 shares of preferred stock designated as Series A Preferred Stock and had 2,093,155 shares of Series A Preferred Stock issued and outstanding. Our board may fix the rights, preferences, privileges and restrictions of our authorized but undesignated preferred shares, including:

- dividend rights and preferences over dividends on our common stock or any series of preferred stock;
- the dividend rate (and whether dividends are cumulative);
- conversion rights, if any;
- voting rights;
- rights and terms of redemption (including sinking fund provisions, if any);
- redemption price and liquidation preferences of any wholly unissued series of any preferred stock and the designation thereof of any of them; and
- to increase or decrease the number of shares of any series subsequent to the issue of shares of that series but not below the number of shares then outstanding.

You should refer to the prospectus supplement relating to the series of preferred stock being offered for the specific terms of that series, including:

- the title of the series and the number of shares in the series;
- the price at which the preferred stock will be offered;

the dividend rate or rates or method of calculating the rates, the dates on which the dividends will be payable, whether or not dividends will be cumulative or noncumulative and, if cumulative, the dates from which dividends on the preferred stock being offered will cumulate;

the voting rights, if any, of the holders of shares of the preferred stock being offered;

the provisions for a sinking fund, if any, and the provisions for redemption, if applicable, of the preferred stock being offered, including any restrictions on the foregoing as a result of arrearage in the payment of dividends or sinking fund installments;

Table of Contents

the liquidation preference per share;

the terms and conditions, if applicable, upon which the preferred stock being offered will be convertible into our common stock, including the conversion price, or the manner of calculating the conversion price, and the conversion period;

the terms and conditions, if applicable, upon which the preferred stock being offered will be exchangeable for debt securities, including the exchange price, or the manner of calculating the exchange price, and the exchange period;

any listing of the preferred stock being offered on any securities exchange;

a discussion of any material federal income tax considerations applicable to the preferred stock being offered;

any preemptive rights;

the relative ranking and preferences of the preferred stock being offered as to dividend rights and rights upon liquidation, dissolution or the winding up of our affairs;

any limitations on the issuance of any class or series of preferred stock ranking senior or equal to the series of preferred stock being offered as to dividend rights and rights upon liquidation, dissolution or the winding up of our affairs; and

any additional rights, preferences, qualifications, limitations and restrictions of the series.

Upon issuance, the shares of preferred stock will be fully paid and nonassessable, which means that its holders will have paid their purchase price in full and we may not require them to pay additional funds.

Any preferred stock terms selected by our board of directors could decrease the amount of earnings and assets available for distribution to holders of our common stock or adversely affect the rights and power, including voting rights, of the holders of our common stock without any further vote or action by the stockholders. The rights of holders of our common stock will be subject to, and may be adversely affected by, the rights of the holders of any preferred stock that may be issued by us in the future. The issuance of preferred stock could also have the effect of delaying or preventing a change in control of our company or make removal of management more difficult.

Series A Preferred Stock

In connection with our registered financing which closed on December 3, 2012, our board of directors designated 2,709,300 of the 5,000,000 authorized shares of preferred stock as our Series A Non-Voting Convertible Preferred Stock, par value $.001 per share.

Rank

The Series A Preferred Stock will rank:

senior to our common stock;

senior to any class or series of our capital stock hereafter created specifically ranking by its terms junior to the Series A Preferred Stock; and

junior to any class or series of our capital stock hereafter created specifically ranking by its terms senior to the Series A Preferred Stock,

Table of Contents

in each case, as to dividends or distributions of assets upon our liquidation, dissolution or winding up whether voluntarily or involuntarily.

Conversion

Each share of Series A Preferred Stock is convertible into one share of our common stock (subject to adjustment as provided in the certificate of designation for the Series A Preferred Stock) at any time at the option of the holder, except that a holder will be prohibited from converting shares of Series A Preferred Stock into shares of common stock if, as a result of such conversion, such holder, together with its affiliates, would beneficially own more than 9.98% of the total number of shares of our common stock then issued and outstanding, which percentage may be increased or decreased by on sixty-five days notice from the holder of Series A Preferred Stock to us.

Liquidation Preference

In the event of our liquidation, dissolution or winding up, holders of Series A Preferred Stock will receive a payment equal to $.001 per share of Series A Preferred Stock before any proceeds are distributed to the holders of our common stock. After the payment of this preferential amount, and subject to the rights of holders of any class or series of our capital stock hereafter created specifically ranking by its terms senior to the Series A Preferred Stock and holders of Series A Preferred Stock will participate ratably in the distribution of any remaining assets with the common stock and any other class or series of our capital stock hereafter created that participates with the common stock in such distributions.

Voting Rights

Shares of Series A Preferred Stock generally have no voting rights, except as required by law and except that the consent of holders of a majority of the outstanding Series A Preferred Stock will be required to amend the terms of the Series A Preferred Stock or the certificate of designation for the Series A Preferred Stock.

Dividends

Holders of Series A Preferred Stock are entitled to receive, and we are required to pay, dividends on shares of the Series A Preferred Stock equal (on an as-if-converted-to-common-stock basis) to and in the same form as dividends (other than dividends in the form of common stock) actually paid on shares of the common stock when, as and if such dividends (other than dividends in the form of common stock) are paid on shares of the common stock.

Redemption

We are not obligated to redeem or repurchase any shares of Series A Preferred Stock. Shares of Series A Preferred Stock are not otherwise entitled to any redemption rights, or mandatory sinking fund or analogous fund provisions.

Listing

There is no established public trading market for the Series A Preferred Stock, and we do not expect a market to develop. In addition, we do not intend to apply for listing of the Series A Preferred Stock on any national securities exchange or trading system.

Fundamental Transactions

If, at any time that shares of Series A Preferred Stock are outstanding, we effect a merger or other change of control transaction, as described in the certificate of designation and referred to as a fundamental transaction, then a holder will have the right to receive, upon any subsequent conversion of a share of Series A Preferred Stock (in lieu of conversion shares) for each issuable conversion share, the same kind and amount of securities, cash or property as such holder would have been entitled to receive upon the occurrence of such fundamental transaction if such holder had been, immediately prior to such fundamental transaction, the holder of one share of common stock.

Table of Contents

Warrants

We may issue warrants for the purchase of our common stock, preferred stock or debt securities or any combination thereof. Warrants may be issued independently or together with our common stock, preferred stock or debt securities and may be attached to or separate from any offered securities. To the extent warrants that we issue are to be publicly-traded, each series of such warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. The warrant agent will act solely as our agent in connection with such warrants. The warrant agent will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. This summary of certain provisions of the warrants is not complete. For the terms of a particular series of warrants, you should refer to the prospectus supplement for that series of warrants and the warrant agreement for that particular series.

Debt Securities

As used in this prospectus, the term debt securities means the debentures, notes, bonds and other evidences of indebtedness that we may issue from time to time. The debt securities will either be senior debt securities, senior subordinated debt or subordinated debt securities. We may also issue convertible debt securities. Debt securities issued under an indenture (which we refer to herein as an Indenture) will be indenture entered into between us and a trustee to be named therein. It is likely that convertible debt securities will not be issued under an Indenture.

The Indenture or forms of Indentures, if any, will be filed as exhibits to the registration statement of which this prospectus is a part. The statements and descriptions in this prospectus or in any prospectus supplement regarding provisions of the Indentures and debt securities are summaries thereof, do not purport to be complete and are subject to, and are qualified in their entirety by reference to, all of the provisions of the Indentures (and any amendments or supplements we may enter into from time to time which are permitted under each Indenture) and the debt securities, including the definitions therein of certain terms.

General

Unless otherwise specified in a prospectus supplement, the debt securities will be direct secured or unsecured obligations of our company. The senior debt securities will rank equally with any of our other unsecured senior and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment to any senior indebtedness.

We may issue debt securities from time to time in one or more series, in each case with the same or various maturities, at par or at a discount. Unless indicated in a prospectus supplement, we may issue additional debt securities of a particular series without the consent of the holders of the debt securities of such series outstanding at the time of the issuance. Any such additional debt securities, together with all other outstanding debt securities of that series, will constitute a single series of debt securities under the applicable Indenture and will be equal in ranking.

Should an indenture relate to unsecured indebtedness, in the event of a bankruptcy or other liquidation event involving a distribution of assets to satisfy our outstanding indebtedness or an event of default under a loan agreement relating to secured indebtedness of our company or its subsidiaries, the holders of such secured indebtedness, if any, would be entitled to receive payment of principal and interest prior to payments on the senior indebtedness issued under an Indenture.

Prospectus Supplement

Each prospectus supplement will describe the terms relating to the specific series of debt securities being offered. These terms will include some or all of the following:

the title of debt securities and whether they are subordinated, senior subordinated or senior debt securities;

Table of Contents

any limit on the aggregate principal amount of debt securities of such series;

the percentage of the principal amount at which the debt securities of any series will be issued;

the ability to issue additional debt securities of the same series;

the purchase price for the debt securities and the denominations of the debt securities;

the specific designation of the series of debt securities being offered;

the maturity date or dates of the debt securities and the date or dates upon which the debt securities are payable and the rate or rates at which the debt securities of the series shall bear interest, if any, which may be fixed or variable, or the method by which such rate shall be determined;

the basis for calculating interest if other than 360-day year or twelve 30-day months;

the date or dates from which any interest will accrue or the method by which such date or dates will be determined;

the duration of any deferral period, including the maximum consecutive period during which interest payment periods may be extended;

whether the amount of payments of principal of (and premium, if any) or interest on the debt securities may be determined with reference to any index, formula or other method, such as one or more currencies, commodities, equity indices or other indices, and the manner of determining the amount of such payments;

the dates on which we will pay interest on the debt securities and the regular record date for determining who is entitled to the interest payable on any interest payment date;

the place or places where the principal of (and premium, if any) and interest on the debt securities will be payable, where any securities may be surrendered for registration of transfer, exchange or conversion, as applicable, and notices and demands may be delivered to or upon us pursuant to the applicable Indenture;

the rate or rates of amortization of the debt securities;

if we possess the option to do so, the periods within which and the prices at which we may redeem the debt securities, in whole or in part, pursuant to optional redemption provisions, and the other terms and conditions of any such provisions;

our obligation or discretion, if any, to redeem, repay or purchase debt securities by making periodic payments to a sinking fund or through an analogous provision or at the option of holders of the debt securities, and the period or periods within which and the price or prices at which we will redeem, repay or purchase the debt securities, in whole or in part, pursuant to such obligation, and the other terms and conditions of such obligation;

the terms and conditions, if any, regarding the option or mandatory conversion or exchange of debt securities;

the period or periods within which, the price or prices at which and the terms and conditions upon which any debt securities of the series may be redeemed, in whole or in part at our option and, if other than by a board resolution, the manner in which any election by us to redeem the debt securities shall be evidenced;

Table of Contents

any restriction or condition on the transferability of the debt securities of a particular series;

the portion, or methods of determining the portion, of the principal amount of the debt securities which we must pay upon the acceleration of the maturity of the debt securities in connection with any event of default if other than the full principal amount;

the currency or currencies in which the debt securities will be denominated and in which principal, any premium and any interest will or may be payable or a description of any units based on or relating to a currency or currencies in which the debt securities will be denominated;

provisions, if any, granting special rights to holders of the debt securities upon the occurrence of specified events;

any deletions from, modifications of or additions to the events of default or our covenants with respect to the applicable series of debt securities, and whether or not such events of default or covenants are consistent with those contained in the applicable Indenture;

any limitation on our ability to incur debt, redeem stock, sell our assets or other restrictions;

the application, if any, of the terms of the applicable Indenture relating to defeasance and covenant defeasance (which terms are described below) to the debt securities;

what subordination provisions will apply to the debt securities;

the terms, if any, upon which the holders may convert or exchange the debt securities into or for our common stock, preferred stock or other securities or property;

whether we are issuing the debt securities in whole or in part in global form;

any change in the right of the trustee or the requisite holders of debt securities to declare the principal amount thereof due and payable because of an event of default;

the depositary for global or certificated debt securities, if any;

any material federal income tax consequences applicable to the debt securities, including any debt securities denominated and made payable, as described in the prospectus supplements, in foreign currencies, or units based on or related to foreign currencies;

any right we may have to satisfy, discharge and defease our obligations under the debt securities, or terminate or eliminate restrictive covenants or events of default in the Indentures, by depositing money or U.S. government obligations with the trustee of the Indentures;

the names of any trustees, depositories, authenticating or paying agents, transfer agents or registrars or other agents with respect to the debt securities;

to whom any interest on any debt security shall be payable, if other than the person in whose name the security is registered, on the record date for such interest, the extent to which, or the manner in which, any interest payable on a temporary global debt security will be paid if other than in the manner provided in the applicable Indenture;

if the principal of or any premium or interest on any debt securities is to be payable in one or more currencies or currency units other than as stated, the currency, currencies or currency units in which it shall be paid and the periods within and terms and conditions upon which such election is to be made and the amounts payable (or the manner in which such amount shall be determined);

Table of Contents

the portion of the principal amount of any debt securities which shall be payable upon declaration of acceleration of the maturity of the debt securities pursuant to the applicable Indenture if other than the entire principal amount;

if the principal amount payable at the stated maturity of any debt security of the series will not be determinable as of any one or more dates prior to the stated maturity, the amount which shall be deemed to be the principal amount of such debt securities as of any such date for any purpose, including the principal amount thereof which shall be due and payable upon any maturity other than the stated maturity or which shall be deemed to be outstanding as of any date prior to the stated maturity (or, in any such case, the manner in which such amount deemed to be the principal amount shall be determined); and

any other specific terms of the debt securities, including any modifications to the events of default under the debt securities and any other terms which may be required by or advisable under applicable laws or regulations.

Unless otherwise specified in the applicable prospectus supplement, the debt securities will not be listed on any securities exchange. Holders of the debt securities may present registered debt securities for exchange or transfer in the manner described in the applicable prospectus supplement. Except as limited by the applicable Indenture, we will provide these services without charge, other than any tax or other governmental charge payable in connection with the exchange or transfer.

Debt securities may bear interest at a fixed rate or a variable rate as specified in the prospectus supplement. In addition, if specified in the prospectus supplement, we may sell debt securities bearing no interest or interest at a rate that at the time of issuance is below the prevailing market rate, or at a discount below their stated principal amount. We will describe in the applicable prospectus supplement any special federal income tax considerations applicable to these discounted debt securities.

We may issue debt securities with the principal amount payable on any principal payment date, or the amount of interest payable on any interest payment date, to be determined by referring to one or more currency exchange rates, commodity prices, equity indices or other factors. Holders of such debt securities may receive a principal amount on any principal payment date, or interest payments on any interest payment date, that are greater or less than the amount of principal or interest otherwise payable on such dates, depending upon the value on such dates of applicable currency, commodity, equity index or other factors. The applicable prospectus supplement will contain information as to how we will determine the amount of principal or interest payable on any date, as well as the currencies, commodities, equity indices or other factors to which the amount payable on that date relates and certain additional tax considerations.

Rights

We may issue rights to purchase our securities. The rights may or may not be transferable by the persons purchasing or receiving the rights. In connection with any rights offering, we may enter into a standby underwriting or other arrangement with one or more underwriters or other persons pursuant to which such underwriters or other persons would purchase any offered securities remaining unsubscribed for after such rights offering. Each series of rights will be issued under a separate rights agent agreement to be entered into between us and one or more banks, trust companies or other financial institutions, as rights agent that we will name in the applicable prospectus supplement. The rights agent will act solely as our agent in connection with the rights and will not assume any obligation or relationship of agency or trust for or with any holders of rights certificates or beneficial owners of rights.

The prospectus supplement relating to any rights that we offer will include specific terms relating to the offering, including, among other matters:

the date of determining the security holders entitled to the rights distribution;

Table of Contents

the aggregate number of rights issued and the aggregate amount of securities purchasable upon exercise of the rights;

the exercise price;

the conditions to completion of the rights offering;

the date on which the right to exercise the rights will commence and the date on which the rights will expire; and

any applicable federal income tax considerations.

Each right would entitle the holder of the rights to purchase for cash the principal amount of securities at the exercise price set forth in the applicable prospectus supplement. Rights may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement. After the close of business on the expiration date, all unexercised rights will become void.

If less than all of the rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than our security holders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby arrangements, as described in the applicable prospectus supplement.

Transfer Agent and Registrar

American Stock Transfer & Trust Company is the transfer agent and registrar for our common stock.

Listing

Our common stock is listed on The NASDAQ Capital Market under the trading symbol BDSI.

Table of Contents

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, direct sales to the public, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

A prospectus supplement or supplements will describe the terms of the offering of the securities, including, to the extent applicable:

- the terms of the offering;
- the name or names of the underwriters, if any;
- the purchase price of the securities or other consideration therefor, and the proceeds, if any, we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents or underwriters compensation;
- any public offering price;
- any discounts or concessions allowed or re-allowed or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters or agents named in the prospectus supplement will be underwriters of or agents for the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered

by any over-allotment option. Any public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities, and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

Table of Contents

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may also make sales through the Internet or through other electronic means. Since we may from time to time elect to offer securities directly to the public, with or without the involvement of agents, underwriters or dealers, utilizing the Internet or other forms of electronic bidding or ordering systems for the pricing and allocation of such securities, you will want to pay particular attention to the description of that system we will provide in a prospectus supplement.

Such electronic system may allow bidders to directly participate, through electronic access to an auction site, by submitting conditional offers to buy that are subject to acceptance by us, and which may directly affect the price or other terms and conditions at which such securities are sold. These bidding or ordering systems may present to each bidder, on a so-called real-time basis, relevant information to assist in making a bid, such as the clearing spread at which the offering would be sold, based on the bids submitted, and whether a bidder s individual bids would be accepted, prorated or rejected. For example, in the case of debt security, the clearing spread could be indicated as a number of basis points above an index treasury note. Of course, many pricing methods can and may also be used.

Upon completion of such an electronic auction process, securities will be allocated based on prices bid, terms of bid or other factors. The final offering price at which securities would be sold and the allocation of securities among bidders would be based in whole or in part on the results of the Internet or other electronic bidding process or auction.

We may provide agents and underwriters with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or in the open market after the distribution is completed, to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters or agents that are qualified market makers on The NASDAQ Capital Market may engage in passive market making transactions in the common stock on The NASDAQ Capital Market in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of our common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker s bid, however, the passive market maker s bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

Table of Contents

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon for us by Ellenoff Grossman & Schole LLP, New York, New York. The legality of the securities for any underwriters, dealers or agents will be passed upon by counsel as may be specified in the applicable prospectus supplement.

EXPERTS

The financial statements and management s assessment of the effectiveness of internal control over financial reporting (which is included in Management s Report on Internal Control over Financial Reporting) incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2014 have been so incorporated in reliance on the report of Cherry Bekaert LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement with the Securities and Exchange Commission under the Securities Act with respect to the shares of our common stock offered by this prospectus. This prospectus is part of that registration statement and does not contain all the information included in the registration statement.

For further information with respect to our common stock and us, you should refer to the registration statement, its exhibits and the material incorporated by reference therein. Portions of the exhibits have been omitted as permitted by the rules and regulations of the Securities and Exchange Commission. Statements made in this prospectus as to the contents of any contract, agreement or other document referred to are not necessarily complete. In each instance, we refer you to the copy of the contracts or other documents filed as an exhibit to the registration statement, and these statements are hereby qualified in their entirety by reference to the contract or document.

The registration statement may be inspected and copied at the public reference facilities maintained by the Securities and Exchange Commission at Room 1024, Judiciary Plaza, 100 F Street, N.E., Washington, D.C. 20549 and the Regional Offices at the Commission located in the Citicorp Center, 500 West Madison Street, Suite 1400, Chicago, Illinois 60661, and at 233 Broadway, New York, New York 10279. Copies of those filings can be obtained from the Commission s Public Reference Section, Judiciary Plaza, 100 F Fifth Street, N.E., Washington, D.C. 20549 at prescribed rates and may also be obtained from the web site that the Securities and Exchange Commission maintains at http://www.sec.gov. You may also call the Commission at 1-800-SEC-0330 for more information. We file annual, quarterly and current reports and other information with the Securities and Exchange Commission. You may read and copy any reports, statements or other information on file at the Commission s public reference room in Washington, D.C. You can request copies of those documents upon payment of a duplicating fee, by writing to the Securities and Exchange Commission.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

We are incorporating by reference certain documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents. The information in the documents incorporated by reference is considered to be part of this prospectus. Statements contained in documents that we file with the SEC and that are incorporated by reference in this prospectus will automatically update and supersede information contained in this prospectus, including information in previously filed documents or reports that have been incorporated by reference in this prospectus, to the extent the new information differs from or is inconsistent with the old information. We have filed or may file the following documents with the SEC and they are incorporated herein by reference as of their respective dates of filing:

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2014, as filed with the SEC on March 16, 2015;

Our Definitive Proxy Statement on Schedule 14(a), as filed with the SEC on June 5, 2015;

Table of Contents

Our Current Reports on Form 8-K, as filed with the SEC on January 28, 2015, February 23, 2015, March 17, 2015, March 30, 2015, May 11, 2015, May 28, 2015 and June 4, 2015;

Our Quarterly Report on Form 10-Q, as filed with the SEC on May 11, 2015;

The description of our common stock contained in our Form 8-A filed on June 19, 2002, as amended June 20, 2002, and as it may be further amended from time to time; and

All documents filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and before the termination or completion of this offering of the securities described in this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part of it from the filing dates of such documents, except in each case for information contained in any such filing where we indicate that such information is being furnished and is not to be considered filed under the Securities Exchange Act of 1934, as amended.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a copy of these filings at no cost (other than exhibits unless such exhibits are specifically incorporated by reference) by writing or telephoning us at the following address and telephone number:

BioDelivery Sciences International, Inc.

4131 ParkLake Avenue, Suite # 225

Raleigh, North Carolina 27612

Telephone: (919) 582-9050

Attention: Ernest R. De Paolantonio

Table of Contents

The information in this prospectus is not complete and may be changed. We may not sell the securities until the Registration Statement filed with the Securities and Exchange Commission, of which this prospectus is a part, is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JULY 2, 2015

PROSPECTUS

Up to $40,000,000 of Shares

Common Stock

We have entered into a sales agreement with Cantor Fitzgerald & Co. relating to shares of our common stock offered by this prospectus. In accordance with the terms of the sales agreement, we may offer and sell up to $40,000,000 of shares of our common stock, $.001 par value per share, from time to time through Cantor Fitzgerald & Co. acting as agent.

Our common stock is listed on The NASDAQ Capital Market under the symbol BDSI. The last reported sale price of our common stock on The NASDAQ Capital Market on June 30, 2015 was $7.96 per share.

Sales of our common stock, if any, under this prospectus may be made in sales deemed to be at-the-market equity offerings as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through The NASDAQ Capital Market, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or any other method permitted by law, including in privately negotiated transactions. Cantor Fitzgerald & Co. will act as sales agent on a best efforts basis and use commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us, consistent with its normal trading and sales practices, on mutually agreed terms between Cantor Fitzgerald & Co. and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Cantor Fitzgerald & Co. will be entitled to compensation at a fixed commission rate of 3.0% of the gross sales price per share sold. In connection with the sale of our common stock on our behalf, Cantor Fitzgerald & Co. will be deemed to be an underwriter within the meaning of the Securities Act and the compensation of Cantor Fitzgerald & Co. will be deemed to be underwriting commissions or discounts.

Investing in our securities involves a high degree of risk. You should read this prospectus and the information incorporated herein by reference carefully before you make your investment decision. See Risk Factors beginning on page S-8 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 2015

Table of Contents

TABLE OF CONTENTS

You should rely only on the information we have provided or incorporated by reference in this prospectus or in any prospectus supplement. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus or in any prospectus supplement.

This prospectus and any prospectus supplement is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so.

You should assume that the information contained in this prospectus and in any prospectus supplement is accurate only as of their respective dates and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any prospective supplement or any sale of securities.

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, utilizing a shelf registration process. Under the shelf registration process, we may offer shares of our common stock having an aggregate offering price of up to $40,000,000 from time to time under this prospectus at prices and on terms to be determined by market conditions at the time of offering.

This prospectus describes the specific terms of the common stock we are offering and also adds to, and updates information contained in the documents incorporated by reference into this prospectus. To the extent there is a conflict between the information contained in this prospectus, on the one hand, and the information contained in any document incorporated by reference into this prospectus that was filed with the SEC before the date of this prospectus, on the other hand, you should rely on the information in this prospectus. If any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference into this prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information contained in, or incorporated by reference into this prospectus and in any free writing prospectus that we may authorize for use in connection with this offering. We have not, and Cantor Fitzgerald & Co. has not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and Cantor Fitzgerald & Co. is not, making an offer to sell or soliciting an offer to buy our securities in any jurisdiction in which an offer or solicitation is not authorized or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus, the documents incorporated by reference into this prospectus, and in any free writing prospectus that we may authorize for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus, the documents incorporated by reference into this prospectus, and any free writing prospectus that we may authorize for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus entitled Where You Can Find More Information and Incorporation by Reference.

We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus outside the United States. This prospectus does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless otherwise stated, all references to us, our, BioDelivery, we, the Company and similar designations refer to BioDelivery Sciences International, Inc. Our logo, trademarks and service marks are the property of BioDelivery Sciences International, Inc. Other trademarks or service marks appearing in this prospectus are the property of their respective holders.

Table of Contents

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement and the documents we have filed or will file with the SEC that are or will be incorporated by reference into this prospectus and the accompanying prospectus supplement contain forward-looking statements, within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended (which we refer to as the Exchange Act), that involve significant risks and uncertainties. Any statements contained, or incorporated by reference, in this prospectus and any accompanying prospectus that are not statements of historical fact may be forward-looking statements. When we use the words anticipate, believe, could, estimate, expect, intend, may, plan, predict, project, will and other similar terms and phrases, including referen 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 our research, development, commercialization, manufacturing, marketing and distribution efforts relating to our BEMA® 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 (iii) 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 BUNAVAIL®, which is the first product we are self-commercializing;
- our ability to generate commercially viable products and the market acceptance of our BEMA® technology platform and our proposed products and product candidates;
- our ability to finance our operations on acceptable terms, either through the raising of capital, the incurrence of convertible or other indebtedness or through strategic financing or commercialization partnerships;
- our expectations about the potential market sizes and market participation potential for our approved or proposed products;
- the protection and control afforded by our patents or other intellectual property, and any interest patents or other intellectual property that we license, 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 (and related activities, including inter-partes reviews and inter-partes reexaminations) or other claims or disputes relating to our business, technologies, products or processes;

our expected revenues (including sales, milestone 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 risks that may impact upon the forward-looking statements used herein or in the documents incorporated by reference herein. Please see Risk Factors in our reports filed with the SEC or in a prospectus supplement related to this prospectus 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 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 prospectus and any accompanying prospectus supplement are based on information available to us on the date hereof or thereof. 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 (or incorporated by reference in) this prospectus, any accompanying prospectus and the documents we have filed with the SEC.

Table of Contents

PROSPECTUS SUMMARY

The following summary highlights selected information contained or incorporated by reference in this prospectus. This summary does not contain all of the information you should consider before investing in the securities. Before making an investment decision, you should read the entire prospectus and any supplement hereto carefully, including the risk factors section as well as the financial statements and the notes to the financial statements incorporated herein by reference.

In this prospectus and any amendment or supplement hereto, unless otherwise indicated, the terms BioDelivery Sciences International, Inc., BDSI, the Company, we, us, and our refer and relate to BioDelivery Sciences International, Inc. and its consolidated subsidiaries.

Overview

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

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

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

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

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

BELBUCA (BEMA® Buprenorphine) for Chronic Pain

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

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

Table of Contents

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

One of the key intellectual property milestones under our Endo Agreement was achieved in February 2012, when the U.S. Patent and Trademark Office (or USPTO) issued a Notice of Allowance regarding one of our patent applications (No. 13/184306) which, once the patent was granted in April 2012, extended the exclusivity of the BEMA® drug delivery technology for BELBUCA (as well as BUNAVAIL®, as discussed below) from 2020 to 2027. As a result, we received a milestone payment from Endo in the amount of $15 million in May 2012, and also related to the issuance of the patent, will receive an additional milestone payment of $20 million at the time of approval of a New Drug Application (or NDA) by the FDA for BELBUCA for the treatment of chronic pain. Such amounts are included in the aforementioned $95 million in potential milestone payments based on intellectual property and clinical development and regulatory events.

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

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

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

On July 7, 2014, we announced with Endo positive top-line results from the Phase 3 efficacy study of BELBUCA in opioid- experienced subjects. The trial successfully met its primary efficacy endpoint in demonstrating that BELBUCA resulted in significantly ($p<0.0001$) improved chronic pain relief compared to placebo. Additional secondary endpoints were supportive of the efficacy of BELBUCA compared to placebo. The

Table of Contents

most commonly reported adverse events in patients treated with BELBUCA compared to placebo were nausea (7.5% vs. 7.4%, respectively) and vomiting (5.5% vs. 2.3%, respectively). Locking of the database for the opioid experienced study triggered an additional $10 million milestone payment from Endo per the terms of the license agreement, which we received July 2014.

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

BUNAVAIL® (buprenorphine and naloxone) buccal film

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

In September 2012, we announced the positive outcome of the pivotal pharmacokinetic study comparing BUNAVAIL® to Suboxone® sublingual tablets. The study was designed to compare the relative bioavailability of buprenorphine and naloxone between BUNAVAIL® and the reference product, Suboxone ® tablets. The results demonstrated that the two key pharmacokinetic parameters, maximum drug plasma concentration (Cmax) and total drug exposure (AUC), for buprenorphine were comparable to Suboxone® sublingual tablet, and that the same parameters for naloxone were similar or less than Suboxone® tablet. This was followed by initiation of the safety study requested by FDA, assessing the safety and tolerability of BUNAVAIL ® in patients converted from a stable dose of Suboxone ® (buprenorphine/naloxone) sublingual tablets or films. A total of 249 patients were enrolled in the study, (191 patients completed) which completed in December 2012. Results of the study showed a very favorable safety and tolerability profile along with strong study subject retention and high dose form acceptability ratings. Data showed that over 91% of patients who switched from Suboxone ® film or tablets considered the taste of BUNAVAIL ® to be very pleasant, pleasant or neutral and over 82% rated the ease of use of BUNAVAIL® as very easy, easy or neutral. The study also showed a decrease in the incidence of constipation symptoms from 41% at baseline, before conversion of patients from Suboxone tablets or films to BUNAVAIL ®, to 13% following 12 weeks of treatment with BUNAVAIL ®.

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

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

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

Table of Contents

ONSOLIS® (fentanyl buccal soluble film)

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

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

We granted commercialization and distribution rights for ONSOLIS® on a worldwide basis (except in South Korea and Taiwan) to Meda. Meda s U.S. subsidiary, Meda Pharmaceuticals, based in Somerset, New Jersey, is a specialty pharmaceutical company that develops, markets and sells branded prescription therapeutics. Meda secured access to additional markets through acquisition of European businesses from Valeant Pharmaceuticals International, Inc., which we refer to herein as Valeant and a joint venture with Valeant covering Australia, Mexico and Canada. In 2010, we secured commercialization rights for ONSOLIS® for the remaining worldwide territories through execution of licensing agreements with KUNWHA Pharmaceutical Co., Ltd. (or Kunwha), for South Korea and TTY Biopharm Co., Ltd. (or TTY) for Taiwan where the product will be marketed as PAINKYL .

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

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

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

Table of Contents

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

Clonidine Topical Gel

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

We believe that the PDN market is highly under-served by existing products and therefore there is a strong scientific rationale for developing a topical treatment for PDN that delivers analgesia in a way that avoids systemic side effects. Evidence has shown that clonidine stimulates an inhibitory receptor in the skin associated with pain fibers. Arcion has assessed its effectiveness in reducing pain in PDN in a double-blind, placebo-controlled, Phase 2 study where the primary study endpoint was the change in pain intensity over a 3 month treatment period in diabetic foot pain. A significant treatment difference was seen in the planned subset analysis of diabetic patients who had documented evidence of functioning pain receptors in the skin of the lower leg (p=0.01, n=63) thus, at a minimum, supporting the effectiveness of topical clonidine in diabetic patients with functioning pain receptors of the skin. In the overall population that included patients without functioning nerve receptors , there was a trend favoring topical Clonidine Topical Gel (p=0.07, n= 182), though the overall results did not reach statistical significance. Oral medications that are approved for the treatment of PDN include anticonvulsants such as Lyrica (pregabalin), the antidepressant Cymbalta ® (duloxetine) and the opioid Nucynta ® ER (tapentadol ER), with sales for the treatment of neuropathic pain totaling over $3 billion in the U.S. according to Datamonitor. These treatments are modestly effective in relieving symptoms and their use can be limited by adverse effects and drug interactions.

In late March 2015, we announced that the primary efficacy endpoint in our Phase 3 clinical study of Clonidine Topical Gel for PDN compared to placebo for the treatment of PDN did not meet statistical significance. Certain secondary endpoints showed statistically significant improvement over the placebo. In addition, a strong safety profile for the product was observed. Based on our ongoing analysis, we believe that the data from this study supports continued development of this product. Our analysis showed an unusually high placebo response in the cohort of patients that entered the trial following our previously announced interim analysis of the study. Generally speaking, we believe there may be study design features that might be able to mitigate this response in all patients that would enter a subsequent study of Clonidine Topical Gel, and we are presently considering these features as we evaluate the potential for additional study of this product candidate. We are therefore currently in the process of determining what the next steps in the development pathway should be and whether our decision may require FDA consultation. One possibility is that we would do a small scale study that takes into account the design features that we believe could mitigate the placebo response we saw in our initial Phase 3 trial. If we decide to pursue this type of study or any next study, it would not likely occur before fourth quarter of 2015.

Buprenorphine Depot Injection

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

Table of Contents

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

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

Additional Information

From our inception through March 31, 2015, we have recorded accumulated losses totaling approximately $213.7 million. Our historical operating losses have resulted principally from our research and development activities, including clinical trial activities for our product candidates and general and administrative expenses. Ultimately, if we secure additional approvals from the FDA and other regulatory bodies throughout the world for our product candidates, our goal will be to augment our current sources of revenue and, as applicable, deferred revenue (principally licensing fees), with sales of such products or royalties from such sales, on which we may pay royalties or other fees to our licensors and/or third-party collaborators as applicable.

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

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

We have based our estimates of development costs, market size estimates, peak annual sales projections and similar matters described below and elsewhere in this prospectus on our market research, third party reports and publicly available information which we consider reliable. However, readers are advised that the projected dates for filing and approval of our INDs or NDAs with the FDA or other regulatory authorities, our estimates of development costs, our projected sales and similar metrics regarding BUNAVAIL ®, ONSOLIS ®, BELBUCA , Clonidine Topical Gel, Buprenorphine Depot Injection or any other product candidates discussed below and elsewhere in this prospectus and any accompanying prospectus supplement 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.

Corporate Information

We are a Delaware corporation. Our executive offices are located at 4131 ParkLake Avenue, Suite 225, Raleigh, North Carolina, 27612, telephone number (919) 582-9050. We maintain an internet website at www.bdsi.com. The information on our website or any other website is not incorporated by reference into this prospectus supplement and does not constitute a part of this prospectus supplement.

Table of Contents

THE OFFERING

Common stock offered by us	Shares of our common stock having an aggregate offering price of up to $40 million.
Common stock to be outstanding after this offering	Up to 57,446,560 shares (as more fully described in the notes following this table), assuming sales at a price of $7.96 per share, which was the closing price of our common stock on The NASDAQ Capital Market on June 30, 2015. The actual number of shares issued will vary depending on the sales price under this offering.
Manner of offering	At-the-market offering that may be made from time to time through our sales agent, Cantor Fitzgerald & Co. See Plan of Distribution on page S-15.
Use of Proceeds	Although we have not yet identified specific uses for the net proceeds we may receive from the sale of any securities offered under this prospectus, we currently anticipate using such proceeds for the clinical and regulatory advancement of our product candidates; for commercialization of our products, including potential sales and marketing of products on our own behalf; to support of our partnered products; for potential acquisitions of new technologies and products, and to meet working capital needs. We are not presently a party to any definitive agreements to make any product or technology acquisitions. We may temporarily invest the net proceeds in investment-grade, interest-bearing securities until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of the net proceeds. See Use of Proceeds on page S-12 of this prospectus.
Risk Factors	Investing in our common stock involves a high degree of risk. Please read the information contained in and incorporated by reference under the heading Risk Factors on page S-8 of this prospectus, and under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus.
NASDAQ Capital Market symbol	BDSI

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 52,421,435 shares outstanding as of the date of this prospectus. The number of shares outstanding as of the date of this prospectus, as used throughout this prospectus, unless otherwise indicated, excludes the following, all as of the date of this prospectus:

2,072,039 shares of our common stock issuable upon exercise of stock options outstanding under our Amended and Restated 2001 Incentive Plan which had at a weighted average exercise price of $4.18 per share and 1,224,438 shares of our common stock issuable upon exercise of stock options outstanding under our 2011 Equity Incentive Plan which had a weighted average exercise price of $7.89 per share;

3,129,950 shares of our common stock issuable upon the vesting of restricted stock units under our 2011 Equity Incentive Plan and 1,043,211 shares of our common stock issuable upon the vesting of restricted stock units under our Performance Long Term Incentive Plan; and

2,093,155 shares of our common stock issuable upon conversion of our outstanding Series A Preferred Stock.

Table of Contents

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should carefully consider the risk factors we describe in any prospectus supplement and in any related free writing prospectus that we may authorize to be provided to you or in any report incorporated by reference into this prospectus or such prospectus supplement, including our Annual Report on Form 10-K for the year ended December 31, 2014, or any Annual Report on Form 10-K or Quarterly Report on Form 10-Q that is incorporated by reference into this prospectus or such prospectus supplement after the date of this prospectus. Although we discuss key risks in those risk factor descriptions, additional risks not currently known to us or that we currently deem immaterial also may impair our business. Our subsequent filings with the SEC may contain amended and updated discussions of significant risks. We cannot predict future risks or estimate the extent to which they may affect our financial performance.

Additional Risks Related to This Offering

Our management will have broad discretion as to the use of the proceeds from this offering, and may not use the proceeds effectively.

Because we have not designated the amount of net proceeds from this offering to be used for any particular purpose, our management will have broad discretion as to the application of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of the offering. Our management may use the net proceeds for corporate purposes that may not improve our financial condition or market value.

You may experience immediate and substantial dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 5,025,125 shares of our common stock are sold during the term of the sales agreement with Cantor Fitzgerald & Co. at a price of $7.96 per share, the last reported sale price of our common stock on The NASDAQ Capital Market on June 30, 2015, for aggregate net proceeds of $38.8 million after deducting commissions and estimated aggregate offering expenses payable by us, you will experience immediate dilution of $6.52 per share, representing the difference between our as adjusted pro forma net tangible book value per share as of December 31, 2014 after giving effect to this offering and the assumed offering price. The exercise of outstanding stock options and warrants may result in further dilution of your investment. See the section entitled Dilution below for a more detailed illustration of the dilution you would incur if you participate in this offering.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

We do not intend to pay dividends in the foreseeable future.

We have never paid cash dividends on our common stock. We currently intend to retain our future earnings, if any, to finance the operation and growth of our business and currently do not plan to pay any cash dividends in the foreseeable future.

Table of Contents

Sales of a significant number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock.

Sales of a significant number of shares of our common stock in the public markets, or the perception that such sales could occur as a result of our utilization of a universal shelf registration statement, our sales agreement with Cantor Fitzgerald & Co. or otherwise could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We cannot predict the effect that future sales of our common stock or the market perception that we are permitted to sell a significant number of our securities would have on the market price of our common stock.

Our stock price is likely to be volatile, and the market price of our common stock may decline in value in the future.

The market price of our common stock has fluctuated in the past and is likely to fluctuate in the future. During the period from January 1, 2013 to March 31, 2015, our stock price has ranged from a low of $3.76 to a high of $18.48. Market prices for securities of pharmaceutical, biotechnology and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the results of our clinical trials;
- the results of clinical trials conducted by others on drugs that would compete with our drug candidates;
- the announcements of those data, particularly at high profile medical meetings, and the investment community s perception of and reaction to those data;
- the ability of our drug candidates to be dosed safely in combination with other drugs and/or drug candidates, both ours and others;
- the entry into, modification of, or termination of key agreements, or any new collaboration agreement we may enter;
- market expectations about the timeliness of our entry into, or failure to enter, collaboration arrangements with third parties;
- the results of regulatory reviews relating to the approval of our drug candidates;
- our failure to obtain patent protection for any of our drug candidates or the issuance of third party patents that cover our drug candidates;
- the initiation of, material developments in, or conclusion of litigation to enforce or defend any of our intellectual property rights;
- failure of any of our drug candidates, if approved, to achieve any level of commercial success;
- general and industry-specific economic conditions that may affect our research and development expenditures;

the launch of drugs by others that would compete with our drug candidates;

the failure or discontinuation of any of our research programs;

issues in manufacturing our drug candidates or any approved products;

Table of Contents

the introduction of technological innovations or new commercial products by us or our competitors;

future sales of our common stock;

period-to-period fluctuations in our financial results;

low trading volume of our common stock;

failure to build a commercial organization in the future to launch our products; and

failure to commercialize any of our products in the future.

In addition, if we fail to reach an important research, development or commercialization milestone or result by a publicly expected deadline, even if by only a small margin, there could be significant impact on the market price of our common stock. Additionally, as we approach the announcement of important clinical data or other significant information and as we announce such results and information, we expect the price of our common stock to be particularly volatile, and negative results would have a substantial negative impact on the price of our common stock.

The stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may adversely affect the trading price of our common stock.

In the past, following periods of volatility in the market price of a company s securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm our business operations and reputation.

Please also read carefully the section above entitled Cautionary Note Regarding Forward-Looking Statements.

Table of Contents

RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth our ratio of fixed charges and preference dividends to earnings for each of the periods indicated. You should read this table in conjunction with the financial statements and notes incorporated by reference in this prospectus.

	For Fiscal Year Ended				
	December 31, 2014	December 31, 2013	December 31, 2012	December 31, 2011	December 31, 2010
Ratios of fixed charges and preference dividends to earnings	N/A	N/A	45.10	N/A	N/A

We have computed the ratio of fixed charges and preference dividends to earnings set forth above by dividing pre-tax loss before fixed charges and preference dividends by fixed charges and preference dividends. Fixed charges are the sum of the following:

- interest expensed and capitalized;
- amortized premiums related to indebtedness; and
- an estimate of the interest within rental expense.

We did not pay any cash dividends on any shares of our capital stock during the periods set forth above.

We did not record earnings for the fiscal years ended December 31, 2014, 2013, 2011 and 2010. Accordingly, our earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of fixed charges and preference dividends to earnings for such periods. The dollar amount of the deficiency in earnings available for fixed charges and preference dividends for the fiscal years ended December 31, 2014, 2013, 2011 and 2010 was approximately $54.2 million, $57.4 million, $23.3 million and $13.0 million, respectively.

Table of Contents

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes. Although we have not yet identified specific uses for these proceeds, we currently anticipate using the proceeds for some or all of the following purposes:

- for the clinical and regulatory advancement of our product candidates;
- for commercialization of our products, including potential sales and marketing of products on our own behalf;
- to support of our partnered products;
- for potential acquisitions of new technologies and products or related companies; and
- to meet working capital needs.

We are not presently a party to any definitive agreements to make any product or technology acquisitions.

The amounts and timing of our use of the net proceeds from this offering will depend on a number of factors, such as the timing and progress of our research and development efforts, the timing and progress of any collaborative or strategic partnering efforts, and the competitive environment for our planned products. Accordingly, our management will have broad discretion in the timing and application of these proceeds. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short-term, interest-bearing instruments.

Table of Contents

DILUTION

If you invest in our common stock, your interest will be diluted immediately to the extent of the difference between the public offering price per share and the adjusted net tangible book value per share of our common stock after this offering.

Our net tangible book value on March 31, 2015 was approximately $43.1 million, or $0.83 per share. Net tangible book value is total assets minus the sum of liabilities and intangible assets. Net tangible book value per share is net tangible book value divided by the total number of shares outstanding.

After giving effect to the sale of shares of our common stock in the aggregate amount of $40 million in this offering at an assumed offering price of $7.96 per share, which was the last reported sale price of our common stock on The NASDAQ Capital Market on June 30, 2015, and after deducting estimated offering commissions and expenses payable by us, our net tangible book value as of March 31, 2015 would have been approximately $81.9 million, or $1.44 per share of common stock. This represents an immediate increase in net tangible book value of $0.61 per share to our existing stockholders and an immediate dilution in net tangible book value of $6.52 per share to investors participating in this offering. The following table illustrates this dilution per share to investors participating in this offering:

Assumed offering price per share		$ 7.96
Net tangible book value per share as of March 31, 2015	$ 0.83	
Increase per share attributable to new investors	$ 0.61	
Net tangible book value per share after giving effect to this offering	$ 1.44	
Dilution per share to new investors		$ 6.52

The table above assumes, for illustrative purposes, that an aggregate of 5,025,125 shares of our common stock are sold at a price of $7.96 per share, the last reported sale price of our common stock on The NASDAQ Capital Market on June 30, 2015, for aggregate gross proceeds of $40 million. The shares sold in this offering, if any, will be sold from time to time at various prices.

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 52,421,435 shares outstanding as of the date of this prospectus. The number of shares outstanding as of the date of this prospectus, as used throughout this prospectus, unless otherwise indicated, excludes the following, all as of the date of this prospectus:

- 2,072,039 shares of our common stock issuable upon exercise of stock options outstanding under our Amended and Restated 2001 Incentive Plan which had at a weighted average exercise price of $4.18 per share and 1,224,438 shares of our common stock issuable upon exercise of stock options outstanding under our 2011 Equity Incentive Plan, as amended which had a weighted average exercise price of $7.89 per share;

- 3,129,950 shares of our common stock issuable upon the vesting of restricted stock units under our 2011 Equity Incentive Plan, as amended and 1,043,211 shares of our common stock issuable upon the vesting of restricted stock units under our Performance Long Term Incentive Plan; and

- 2,093,155 shares of our common stock issuable upon conversion of our outstanding Series A Preferred Stock.

To the extent that any of our outstanding options or warrants are exercised, we grant additional options or other awards under our stock incentive plan or issue additional warrants, or we issue additional shares of common stock in the future, there may be further dilution.

Table of Contents

PRICE RANGE OF COMMON STOCK

Our common stock is listed on The NASDAQ Capital Market under the symbol BDSI. The following table shows the high and low per share sale prices of our common stock for the periods indicated.

	High	Low
Fiscal Year Ended December 31, 2013		
1st Quarter	$ 4.85	$ 3.76
2nd Quarter	5.68	3.96
3rd Quarter	5.55	4.05
4th Quarter	5.83	4.24
Fiscal Year Ended December 31, 2014		
1st Quarter	$ 10.20	$ 5.65
2nd Quarter	12.81	6.71
3rd Quarter	18.48	11.76
4th Quarter	18.33	11.48
Fiscal Year Ending December 31, 2015		
1st Quarter	$ 15.50	$ 9.32

On June 30, 2015, the last sale price reported on The NASDAQ Capital Market for our common stock was $7.96 per share.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock. We currently intend to retain earnings, if any, to support our business strategy and do not anticipate paying cash dividends in the foreseeable future. Payment of future dividends, if any, will be at the sole discretion of our board of directors after taking into account various factors, including our financial condition, operating results, capital requirements and any plans for expansion.

Table of Contents

PLAN OF DISTRIBUTION

We have entered into a Controlled Equity Offering[SM] sales agreement with Cantor Fitzgerald & Co. pursuant to which we may issue and sell up to an aggregate of $40 million of shares of our common stock, par value $0.001 per share, from time to time through Cantor Fitzgerald & Co. acting as agent. A copy of the sales agreement has been filed as an exhibit to the registration statement of which this prospectus forms a part.

Upon delivery of a placement notice and subject to the terms and conditions of the sales agreement, Cantor Fitzgerald & Co. may sell our common stock by any method permitted by law deemed to be an at-the-market offering as defined in Rule 415 promulgated under the Securities Act, including sales made directly on The NASDAQ Capital Market, on any other existing trading market for our common stock or to or through a market maker. Cantor Fitzgerald & Co. may also sell our common stock by any other method permitted by law, including in privately negotiated transactions. We or Cantor Fitzgerald & Co. may suspend or terminate the offering of our common stock upon notice and subject to other conditions.

We will pay Cantor Fitzgerald & Co. in cash, upon each sale of our common stock pursuant to the sales agreement, a commission in an amount equal to 3.0% of the aggregate gross proceeds from each sale of our common stock. Because there is no minimum offering amount required as a condition to this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We have agreed, under certain circumstances, to reimburse a portion of Cantor Fitzgerald & Co. s expenses, including legal fees, in connection with this offering up to a maximum of $50,000. We estimate that the total expenses for the offering, excluding compensation and expense reimbursement payable to Cantor Fitzgerald & Co. under the terms of the sales agreement, will be approximately $100,000.

Settlement for sales of common stock will occur on the third business day following the date on which any sales are made, or on some other date that is agreed upon by us and Cantor Fitzgerald & Co. in connection with a particular transaction, in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement. Sales of our common stock as contemplated in this prospectus will be settled through the facilities of The Depository Trust Company or by such other means as we and Cantor Fitzgerald & Co. may agree upon.

Cantor Fitzgerald & Co. will act as sales agent on a commercially reasonable efforts basis consistent with its normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of The NASDAQ Capital Market. In connection with the sale of the common stock on our behalf, Cantor Fitzgerald & Co. will be deemed to be an underwriter within the meaning of the Securities Act and the compensation of Cantor Fitzgerald & Co. will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to Cantor Fitzgerald & Co. against certain civil liabilities, including liabilities under the Securities Act.

The offering of our common stock pursuant to the sales agreement will terminate upon the termination of the sales agreement as permitted therein. We and Cantor Fitzgerald & Co. may each terminate the sales agreement at any time upon 10 days prior notice.

Cantor Fitzgerald & Co. and its affiliates may in the future provide various investment banking, commercial banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees. To the extent required by Regulation M, Cantor Fitzgerald & Co. will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus.

This prospectus in electronic format may be made available on a web site maintained by Cantor Fitzgerald & Co. and Cantor Fitzgerald & Co. may distribute this prospectus electronically.

Table of Contents

LEGAL MATTERS

The validity of the issuance of the common stock offered by this prospectus will be passed upon for us by Ellenoff Grossman & Schole LLP, New York, New York. Cantor Fitzgerald & Co. is being represented in connection with this offering by Reed Smith LLP, New York, New York.

EXPERTS

The financial statements and management s assessment of the effectiveness of internal control over financial reporting (which is included in Management s Report on Internal Control over Financial Reporting) incorporated in this prospectus supplement by reference to the Annual Report on Form 10-K for the year ended December 31, 2014 have been so incorporated in reliance on the report of Cherry Bekaert LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC s website at http://www.sec.gov. You may also read and copy any document we file at the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

We are incorporating by reference certain documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents. The information in the documents incorporated by reference is considered to be part of this prospectus supplement. Statements contained in documents that we file with the SEC and that are incorporated by reference in this prospectus supplement will automatically update and supersede information contained in this prospectus supplement, including information in previously filed documents or reports that have been incorporated by reference in this prospectus supplement, to the extent the new information differs from or is inconsistent with the old information. We have filed or may file the following documents with the SEC and they are incorporated herein by reference as of their respective dates of filing:

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2014, as filed with the SEC on March 16, 2015;

Our Definitive Proxy Statement on Schedule 14(a), as filed with the SEC on June 5, 2015;

Our Current Reports on Form 8-K, as filed with the SEC on January 28, 2015, February 23, 2015, March 17, 2015, March 30, 2015, May 11, 2015, May 28, 2015 and June 4, 2015;

Our Quarterly Report on Form 10-Q, as filed with the SEC on May 11, 2015;

The description of our common stock contained in our Form 8-A filed on June 19, 2002, as amended June 20, 2002, and as it may be further amended from time to time; and

All documents filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement and before the termination or completion of this offering of the securities described in this prospectus supplement shall

be deemed to be incorporated by reference in this prospectus supplement and to be a part of it from the filing dates of such documents, except in each case for information contained in any such filing where we indicate that such information is being furnished and is not to be considered filed under the Securities Exchange Act of 1934, as amended.

Table of Contents

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a copy of these filings at no cost (other than exhibits unless such exhibits are specifically incorporated by reference) by writing or telephoning us at the following address and telephone number:

BioDelivery Sciences International, Inc.

4131 ParkLake Avenue, Suite # 225

Raleigh, North Carolina 27612

Telephone: (919) 582-9050

Attention: Ernest R. De Paolantonio

Table of Contents

Up to $40,000,000 of Shares

Common Stock

PROSPECTUS

, 2015

Table of Contents

PART II

INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth an estimate of the fees and expenses, other than the underwriting discounts and commissions, payable by the Registrant in connection with the issuance and distribution of the securities being registered.

	Amount
SEC registration fee	$ 17,430.00
Accounting fees and expenses	*
Legal fees and expenses	*
NASDAQ Listing fees	*
Miscellaneous fees and expenses	*
Total	*

* These fees are calculated based on the securities offered and the number of issuances and accordingly cannot be estimated at this time.

Item 15. Indemnification of Directors and Officers

Our certificate of incorporation provides that all our directors, officers, employees and agents shall be entitled to be indemnified by us to the fullest extent permitted under the Delaware General Corporation Law, provided that they acted in good faith and that they reasoned their conduct or action was in, or not opposed to, the best interest of our company.

Our Amended and Restated Bylaws provide for indemnification of our officers, directors and others who become a party to an action on our behalf by us to the fullest extent not prohibited under the Delaware General Corporation Law. Further, we maintain officer and director liability insurance.

The underwriting agreement(s) that we may enter into in connection with the securities being offered under this registration statement may provide for indemnification by any underwriters used by us, our directors, our officers who sign the registration statement and our controlling persons for some liabilities, including liabilities arising under the Securities Act.

Item 16. Exhibits

The following exhibits are filed with this registration statement.

Exhibit Number	Description of Document
1.1	Form of Underwriting Agreement[5]
1.2	Controlled Equity Offering[SM] Sales Agreement with Cantor Fitzgerald & Co., dated July 2, 2015*
3.1	Certificate of Incorporation of the Company[1]
3.2	Amended and Restated Bylaws of the Company[2]
3.3	Certificate of Amendment to the Company s Certificate of Incorporation creating a staggered board of directors, dated July 25, 2008[3]

3.4	Certificate of Amendment to the Company s Certificate of Incorporation increasing the number of authorized shares, dated July 22, 2011[4]
4.1	Form of Indenture*
4.2	Form of Debt Securities[5]

Table of Contents

Exhibit Number	Description of Document
4.3	Form of Warrant Agreement, if any, including form of Warrant(5)
4.4	Form of Common Stock Certificate(6)
4.4	Form of Preferred Stock Certificate(5)
4.5	Form of Right Certificate (5)
4.6	Form of Unit Agreement(5)
5.1	Opinion of Ellenoff Grossman & Schole LLP*
23.1	Consent of Cherry Bekaert LLP*
23.2	Consent of Ellenoff Grossman & Schole LLP (included in Exhibit 5.1)*
24.1	Power of Attorney (included in Part II of this Registration Statement)*
25.1	Statement of Eligibility of trustee on Form T-1+

* Filed herewith.
\+ To be filed pursuant to Rule 305(b)(2) of the Trust Indenture Act.
(1) Previously filed with Form SB-2, Amendment No. 2, February 1, 2002.
(2) Previously filed with Form 8-K, July 23, 2010.
(3) Previously filed with Form 8-K, July 28, 2008.
(4) Previously filed with Form 8-K, dated July 25, 2011.
(5) If applicable, to be filed by amendment or by a report filed under the Exchange Act, and incorporated herein by reference.
(6) Previously filed with Form SB-2, Amendment No. 6 on June 18, 2002.

Item 17. Undertakings

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) to include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement; and

(iii) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, *however*, that paragraphs (1)(i), (1)(ii) and (1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

Table of Contents

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(5) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(6) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability of the registrant under the Securities Act of 1933, each filing of the registrant s annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan s annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Table of Contents

(h) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

(j) The undersigned registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the Commission under Section 305(b)(2) of the Trust Indenture Act.

Table of Contents

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Raleigh, State of North Carolina, on July 2, 2015.

BIODELIVERY SCIENCES INTERNATIONAL, INC.

By: /s/ Mark A. Sirgo
Name: Mark A. Sirgo
Title: President and Chief Executive Officer

KNOW ALL MEN BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Mark A. Sirgo and Ernest R. De Paolantonio, or either of them, as his true and lawful attorneys-in-fact and agents, with full power of substitution and substitution, for him or her and in his or her name, place and stead, in any and all capacities, to file and sign any and all amendments, including pre-effective and post-effective amendments, and any registration statement for the same offering that is to be effective under Rule 462(b) of the Securities Act, to this registration statement, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their substitute or substitutes may lawfully do or cause to be done by virtue hereof. This power of attorney shall be governed by and construed with the laws

In accordance with the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities and on the dates stated.

Person	Capacity	Date
/s/ Francis E. O Donnell, Jr. Francis E. O Donnell, Jr.	Executive Chairman	July 2, 2015
/s/ Mark A. Sirgo Mark A. Sirgo	President and Chief Executive Officer (Principal Executive Officer)	July 2, 2015
/s/ Ernest R. De Paolantonio Ernest R. De Paolantonio	Chief Financial Officer, Treasurer and Secretary (Principal Financial Officer and Principal Accounting Officer)	July 2, 2015
/s/ William B. Stone William B. Stone	Lead Director	July 2, 2015
/s/ John J. Shea John J. Shea	Director	July 2, 2015
/s/ Samuel P. Sears, Jr. Samuel P. Sears, Jr.	Director	July 2, 2015
/s/ Thomas W. D Alonzo	Director	July 2, 2015

Thomas W. D Alonzo		
/s/ Charles J. Bramlage Charles J. Bramlage	Director	July 2, 2015
/s/ Barry I. Feinberg, M.D Barry I. Feinberg, M.D.	Director	July 2, 2015