Fibrocell Science, Inc.
Form 10-K
March 10, 2016

UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

ý Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934
For the fiscal year ended December 31, 2015
OR
¨ Transition Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Fibrocell Science, Inc.
(Exact name of registrant as specified in its Charter.)

Delaware	001-31564	87-0458888
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

405 Eagleview Boulevard
Exton, Pennsylvania 19341
(Address of principal executive offices, including zip code)
(484) 713-6000
(Registrant's telephone number, including area code)
Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of each exchange on which registered
Common Stock, $.001 par value	The NASDAQ Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act: None

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Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No ý
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No ý
Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ý No o
Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ý No o
Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ý
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 ¨

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

The aggregate market value of the registrant's common stock held by non-affiliates was $134.9 million as of June 30, 2015 (the last business day of the registrant's most recently completed second fiscal quarter), based on a total of 25,594,501 shares of common stock held by non-affiliates and on a closing price of $5.27 as reported on NASDAQ on June 30, 2015.

As of March 4, 2016, there were 43,898,785 shares of the registrant's common stock, par value $0.001 per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2016 annual meeting of stockholders are incorporated by reference into Part III of this Form 10-K where indicated. Such definitive proxy statement will be filed with the U.S. Securities and Exchange Commission within 120 days after the year ended December 31, 2015.

TABLE OF CONTENTS

Unless the context otherwise indicates, references in this Form 10-K to "Fibrocell," "the Company," "we," "us" and "our" refer to Fibrocell Science, Inc. and its subsidiaries.

Fibrocell, Fibrocell Science and LAVIV® are trademarks of Fibrocell. Other trademarks, trade names and service marks appearing in this Form 10-K are the property of their respective owners.

Table of Contents

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Form 10-K contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. These statements include, among others, statements about:

- the sufficiency of our cash and cash equivalents to fund our operations into the fourth quarter of 2016;
- our ability to obtain additional capital in sufficient amounts and on terms acceptable to us, and the consequences of failing to do so;
- future expenses and capital expenditures;
- our expectation to announce primary endpoint results of our Phase II clinical trial for azficel-T in the second quarter of 2016;
- our interpretation of the U.S. Food and Drug Administration's ("FDA") feedback relating to our Investigational New Drug ("IND") application for FCX-007 and our plans to address such feedback and submit an amended IND in the first quarter of 2016;
- the initiation, design and timing of our planned Phase I/II clinical trial for FCX-007;
- our expectation to submit an IND for FCX-013 to the FDA in 2017;
- the implication of results from pre-clinical and clinical trials and other research activities;
- our ability to obtain orphan drug designation for FCX-013;
- our ability to complete, or obtain modifications to, the postmarketing study required by the FDA for LAVIV;
- the potential advantages of our product candidates and technologies;
- the scope and duration of intellectual property protection; and
- the effect of legal and regulatory developments;

as well as other statements relating to our future operations, financial performance or financial condition, prospects or other future events. Forward-looking statements appear primarily in the sections of this Form 10-K entitled “Item 1—Business,” “Item 1A—Risk Factors,” “Item 7—Management's Discussion and Analysis of Financial Condition and Results Operations,” “Item 7A—Quantitative and Qualitative Disclosures About Market Risk,” and “Item 8—Financial Statements and Supplementary Data.” In some cases, you can identify forward-looking statements by words such as “may,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “scheduled” and similar expressions, although not all forward-looking statements contain these identifying words.

Forward-looking statements are based upon current expectations and assumptions and are subject to a number of known and unknown risks, uncertainties and other factors that could cause actual results to differ materially and adversely from those expressed or implied by such statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in this Form 10-K and in particular the risks and uncertainties discussed under "Item 1A—Risk Factors" of this Form 10-K. As a result, you should not place undue reliance on forward-looking statements.

Additionally, the forward-looking statements contained in this Form 10-K represent our views only as of the date of this Form 10-K (or any earlier date indicated in such statement). While we may update certain forward-looking statements from time to time, we specifically disclaim any obligation to do so, even if new information becomes available in the future.

The foregoing cautionary statements are intended to qualify all forward-looking statements wherever they may appear in this Form 10-K. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

This Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ

materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

Table of Contents

Part I
Item 1. Business
Overview

We are an autologous cell and gene therapy company translating personalized biologics into medical breakthroughs. Our approach to personalized biologics is distinctive. We target the underlying cause of disease by using fibroblast cells from a patient's skin to create localized therapies—with or without genetic modification—that are compatible with the unique biology of the patient.

We are focused on discovering and developing localized therapies for diseases affecting the skin, connective tissue and joints to improve the lives of patients and their families. In that regard, we commit significant resources to our research and development programs. Currently, all of our research and development operations and focus are on gaining regulatory approvals to commercialize our product candidates in the United States, however, we may seek to expand into foreign markets in the future.

Our current pre-clinical and clinical development program pipeline consists of the following product candidates:

Table of Contents

Our most advanced development program is azficel-T for the treatment of vocal cord scarring resulting in chronic or severe dysphonia. We are currently investigating this indication in a Phase II clinical trial. We have completed dosing in this trial and expect to announce primary endpoint results in the second quarter of 2016.

In collaboration with Intrexon Corporation ("Intrexon"), we have two gene-therapy product candidates in pre-clinical development and a third gene-therapy program in the research phase. Our lead gene-therapy product candidate, FCX-007, is in late-stage pre-clinical development for the treatment of recessive dystrophic epidermolysis bullosa (“RDEB”). RDEB is a devastating, rare, congenital, painful, progressive, blistering skin disease that often leads to premature death. FCX-007 has received orphan drug designation as well as rare pediatric disease designation from the FDA. Our second gene-therapy product candidate, FCX-013, is in pre-clinical development for the treatment of linear scleroderma. Linear scleroderma is a localized autoimmune skin disorder that manifests as excess production of extracellular matrix that causes tightening and hardening of the skin and is characterized by linear areas of fibrosis, or skin thickening. We plan to seek orphan drug designation for FCX-013. Our third gene-therapy program is focused on the treatment of arthritis and is in the research phase.

Our Strategy

Our strategy is to develop and commercialize transformational therapies for diseases affecting the skin, connective tissue and joints to improve the lives of patients and their families. Key elements of our strategy are:

- Leveraging our FDA-approved BLA for azficel-T to investigate and seek approval for additional therapeutic indications, including but not limited to vocal cord scarring resulting in chronic or severe dysphonia;
- Advancing our gene-therapy product candidates, FCX-007 and FCX-013, into human clinical trials;
- Advancing our gene-therapy program focused on arthritis through research and into pre-clinical development; and
- Leveraging our FDA-inspected, cGMP manufacturing facility and our expertise in cell therapy manufacturing to advance the development of our autologous cell and gene therapy pipeline.

Our Personalized Biologics Platform

The foundation of our personalized biologics platform is our proprietary autologous fibroblast technology. Fibroblasts are the most common cell in skin and connective tissue and are responsible for synthesizing extracellular matrix proteins, including collagen and other growth factors, that provide structure and support. Because fibroblasts naturally reside in the localized environment of the skin and connective tissue, they represent an ideal therapeutic agent for the treatment of diseases affecting the skin, connective tissue and joints. Utilizing our autologous fibroblast technology, we use a patient's fibroblast cells to create therapies—with or without genetic modification—that are compatible with the unique biology of the patient (i.e., autologous).

Table of Contents

One Powerful Platform Drives Two Product Engines

Our personalized biologics platform is comprised of two separate product engines, each of which uses our proprietary autologous fibroblast technology.

Autologous Fibroblast Product Engine

Our Autologous Fibroblast Product Engine utilizes fibroblast cells to uniquely target the localized environment of skin and connective tissue, which are generally difficult to treat with systemic drug therapies due to limited blood flow to these areas. In 2011, we obtained FDA-approval of LAVIV (azficel-T). LAVIV uses autologous fibroblast cells to improve the appearance of moderate to severe nasolabial fold wrinkles in adults. Although we shifted our strategic focus away from the aesthetics market in 2013, we are leveraging our FDA-approved biologics license application ("BLA") for LAVIV to investigate the use of azficel-T in other therapeutics areas. Currently, we are investigating azficel-T in a Phase II clinical trial for the treatment of vocal cord scarring resulting in chronic or severe dysphonia.

Gene Therapy Product Engine

Our Gene Therapy Product Engine integrates our autologous fibroblast technology with the synthetic biology technology of our collaborator, Intrexon. By combining these technologies, we are genetically modifying autologous fibroblast cells to express targeted proteins in order to address the underlying cause of debilitating diseases affecting the skin, connective tissue and joints. Through our collaboration with Intrexon, we have access to:

- Intrexon’s proprietary vector technology, which is designed to facilitate the assembly and delivery of the necessary target gene constructs for delivery to autologous fibroblast cells. Access to this technology allows us to rapidly screen and construct genetic therapeutic solutions.

Table of Contents

- Intrexon's proprietary RheoSwitch Therapeutic System® (RTS®) technology. The RTS® biologic switch is activated by an orally-administered compound that provides the ability to control level and timing of protein expression in those diseases where such control is ideal.

Currently, we have two gene-therapy product candidates in pre-clinical development, FCX-007 for the treatment of RDEB and FCX-013 for the treatment of linear scleroderma. A third gene-therapy program, focused on the treatment of arthritis, is in the research phase.

Advantages of Our Approach

We believe our personalized biologics approach provides the following distinct advantages for creating cell and gene therapies:

- Localized administration—avoids side effects typically associated with systemic therapy
- Reduced rejection concerns—because autologous fibroblasts are compatible with the unique biology of each patient
- Fibroblast cells are genetically modified ex vivo—to enable testing for safety and confirmation of protein expression levels prior to administration to the patient
- Demonstrated expertise in manufacturing our fibroblast cell therapy

Development Programs

Our development programs are focused on diseases affecting the skin, connective tissue and joints for which there are high unmet needs. Our programs consist of the following:

Program	Potential Indication	Status
azficel-T	Vocal Cord Scarring resulting in Chronic or Severe Dysphonia	Phase II Clinical Trial
FCX-007	RDEB	Pre-clinical
FCX-013	Linear Scleroderma	Pre-clinical
New Gene Therapy Program	Arthritis	Research

azficel-T for Vocal Cord Scarring

Vocal cord scarring is caused by damage to the fibroblast layer of the vocal cords which reduces vocal cord elasticity and airflow, affecting voice tone and volume. This reduction in vocal capacity is referred to as dysphonia, severe cases of which can lead to a total loss of voice. Current treatments for vocal cord scarring, which include voice therapy and surgery through the use of injection (collagen, fat, calcium, hyaluronic acid) or implant (PTFE, silastic), only address the symptoms of vocal cord scarring and have inconsistent efficacy.

azficel-T is in development to treat patients suffering from vocal cord scarring that is either idiopathic or age-related, of which we estimate there to be approximately 64,000 in the U.S. We believe azficel-T restores the extracellular matrix to repair damage to the fibroblast layer of the vocal cords, thereby improving voice quality. This program is being conducted under an IND that cross-references our FDA-approved BLA for LAVIV, which allows us to leverage the safety, chemistry and manufacturing data contained in the BLA.

Phase I Trial

In our Phase I open label clinical trial of azficel-T for the treatment of vocal cord scarring resulting in chronic or severe dysphonia, we examined the safety and efficacy of azficel-T injections for patients who had failed to improve following currently available treatments. Five patients were treated in the clinical trial. For patients with only one impacted vocal cord, azficel-T was injected into the vocal cord over three separate injection sessions approximately 28 days apart. For patients with both vocal cords impacted, azficel-T was injected into the vocal cords over six separate

injection sessions approximately 14 days apart, alternating vocal cords at each injection session.

The voice quality of each patient was evaluated using Mucosal Wave Grade assessment, Voice Handicap Index and patient-assessed voice quality prior to treatment and at 4 and 12 months following treatment. For the Mucosal Wave Grade assessment, each patient phonates a sustained vowel while the vocal cord vibration is recorded using a videostroboscope. The

Table of Contents

recording is then assessed and scored on a 1 (no wave present) to 5 (normal wave) scale. The pliability of the vocal cords can be visualized as waves of mucosa on the vocal cord surface during vibration. The deficiency of the vocal cord tissue results in lack of pliability of the cord, resulting in a reduction of score. The Voice Handicap Index is a questionnaire to quantify the functional, physical and emotional impacts of a voice disorder on a patient's quality of life. The scale contains 30 items in three categories, scored 0 (never) to 4 (always) per item. An 18-point reduction in the overall Voice Handicap Index score is considered to be a significant change in voice quality.

The data from this trial showed a positive trend of sustained improvement in a majority of the patients in the Mucosal Wave Grade assessment and Voice Handicap Index. The mean results for all patients are set forth below:

Mucosal Wave Grade
Mean baseline result = 1.3
Mean 4-month result = 3 (1.7 improvement over baseline)
Mean 12-month result = 3.22 (1.92 improvement over baseline)

Voice Handicap Index
Mean baseline result = 83.8
Mean 4-month result = 55.8 (-28 improvement over baseline)
Mean 12-month result = 52.6 (-31.2 improvement over baseline)

No serious adverse events were reported in the study. Three of the five patients reported ear pain with a majority of the cases being mild or severe in severity. Voice alternation was noted in one subject with a duration of one day, and was categorized as possibly related to treatment. All other reported adverse events were considered to be unrelated to the study treatment and there were no laboratory abnormalities or other untoward events that were considered related to study treatment. Based on these results, azficel-T was well-tolerated in this patient population.

Phase II Trial

Our Phase II clinical trial that is currently in progress is a double-blind, randomized, placebo-controlled trial that is designed to test the safety and efficacy of azficel-T injections in patients with chronic dysphonia caused by vocal cord scarring or atrophy. In this clinical trial, patients were administered the same dose at the same time intervals as in the Phase I clinical trial. We have completed dosing for all 21 patients currently enrolled in the trial. Efficacy endpoints will be assessed four months after administration of final treatment on three different scales: Voice Handicap Index, Mucosal Wave Grade, and GRBAS (grade, roughness, breathiness, asthenia & strain). For GRBAS, a recording of the patient's voice is assessed for grade, roughness, breathiness, asthenia and strain, and scored on a four-point scale where, 0 = normal, 1 = mild, 2= moderate, and 3 = severe. We expect to report primary endpoint results in the second quarter of 2016. As of March 8, 2016, no treatment-related serious adverse events have been reported.

FCX-007 for RDEB

Recessive dystrophic epidermolysis bullosa is a congenital, progressive, devastatingly painful and debilitating genetic disorder that often leads to death, and is the most severe form of dystrophic epidermolysis bullosa. RDEB is caused by a mutation of the COL7A1 gene. The COL7A1 gene encodes for type VII collagen (“COL7”), a protein that forms anchoring fibrils. Anchoring fibrils hold together the layers of skin, and without them, skin layers separate causing severe blistering, open wounds and scarring in response to any kind of friction, including normal daily activities like rubbing or scratching. Children who inherit this condition are often called “butterfly children” because their skin can be as fragile as a butterfly’s wings. We estimate that there are approximately 1,100 - 2,500 people suffering from RDEB in the U.S. Current treatments for RDEB, which include daily bandaging, hydrogel dressings, antibiotics, feeding tubes, and surgery (hand and esophageal), only address the symptoms of the disorder.

6

Table of Contents

Our lead gene-therapy product candidate, FCX-007, is in pre-clinical development for the treatment of RDEB. FCX-007 is an autologous fibroblast cell genetically modified to express COL7 for localized treatment of RDEB. FCX-007 is designed to be delivered to the dermal layer where the genetically-modified fibroblast cells will produce COL7 to promote the formation of anchoring fibrils to aid in wound closure and prevention of wound recurrence. We are developing FCX-007 in collaboration with Intrexon.

FCX-007 was evaluated for toxicology and biological proof-of-concept in RDEB and normal human skin xenografts implanted onto severe combined immunodeficiency (SCID) mice. Toxicology results for FCX-007 showed, at two- and six-weeks post-administration, that there were:

- No treatment-related findings;
- No tumors in the skin grafts or other organs;
- No statistical changes in blood chemistry; and
- No apparent systemic distribution of the vector.

In addition, data supporting the biological proof-of-concept indicated FCX-007 cells in a human skin xenograft SCID mice model expressed COL7 that localized to the basement membrane zone where anchoring fibrils are formed suggesting that the biological mechanism of action of FCX-007 was verified.

We submitted an IND for FCX-007 to the FDA in July 2015. In September 2015, we received feedback from the FDA on the IND which required us to delay the initiation of our proposed Phase I/II clinical trial. The FDA's feedback related to the areas of chemistry, manufacturing and controls, toxicology and our proposed Phase I/II clinical trial protocol. Although the hybrid pharmacology/toxicology study performed based on the injection of FCX-007 into human skin that was xenografted onto SCID mice was included in the IND and showed no signs of toxicity, the FDA requested that we execute a toxicology-specific study in which FCX-007 is injected in non-grafted SCID mice. We have initiated this new toxicology study, and we expect to amend the IND in response to the FDA's feedback and to include data from the new study in the first quarter of 2016. Subject to successful completion of the new toxicology study and satisfactorily addressing the FDA's other feedback, we expect to initiate a Phase I/II clinical trial for FCX-007 in the second quarter of 2016.

FCX-013 for Linear Scleroderma

Linear scleroderma is a localized autoimmune skin disorder that manifests as excess production of extracellular matrix, specifically type I collagen and type III collagen, resulting in fibrosis and linear scars. The linear areas of skin thickening may extend to underlying tissue and muscle in children which may impair growth and development. Lesions appearing across joints can be painful, impair motion and may be permanent. Current treatments for linear scleroderma, which include systemic or topical corticosteroids, UVA light therapy and physical therapy, only address the symptoms of the disorder. We estimate the U.S. population of patients who have linear scleroderma over a major joint and exhibit severe joint pain to be approximately 40,000.

Our second gene-therapy product candidate, FCX-013, is in pre-clinical development for the treatment of linear scleroderma. FCX-013 is an autologous fibroblast cell genetically modified to express a protein to breakdown collagen accumulation at the site of the localized disease. FCX-013 incorporates Intrexon's proprietary RTS® switch, a biologic switch activated by an orally administered compound to control protein expression once the initial fibrosis has been resolved.

Table of Contents

FCX-013 is designed to be injected under the skin at the location of the fibrosis where the genetically-modified fibroblast cells will produce a protein to break down excess collagen accumulation. The patient takes an oral compound to facilitate protein expression. Once the fibrosis is resolved, the patient will stop taking the oral compound which will stop further production of the subject protein by FCX-013.

We have successfully completed a proof-of-concept study for FCX-013 in which the primary objective was to determine whether FCX-013 had the potential to reduce dermal thickness in fibrotic tissue. In this study, FCX-013 was evaluated in a bleomycin-induced scleroderma model utilizing SCID mice. Data from the study demonstrated that FCX-013 reduced dermal thickness of fibrotic tissue to levels similar to that of the non-treated control and further reduced the thickness of the sub-dermal muscle layer. FCX-013 will now be advanced into dose-ranging and toxicology/biodistribution studies for product optimization. We expect to submit an IND for FCX-013 to the FDA in 2017.

New Gene Therapy Program for Arthritis

Arthritis is a broad term that covers a group of more than 100 different types of diseases that affect the joints, as well as connective tissues and organs, including the skin. According to the Centers for Disease Control and Prevention, arthritis—characterized by joint inflammation, pain, and decreased range of motion—is the United States' most common cause of disability affecting more than 52 million adults as well as 300,000 children at a cost exceeding $120 billion.

Our third gene-therapy program is focused on the treatment of arthritis. This program is in the research phase and is being undertaken in collaboration with Intrexon. Our goal is to deliver a protein therapy locally to the joint to provide sustained efficacy while avoiding key side effects typically associated with systemic therapy.

Commercial Program

LAVIV (azficel-T) for Nasolabial Fold Wrinkles

LAVIV (azficel-T) was approved by the FDA in June 2011 for the improvement of the appearance of moderate to severe nasolabial fold wrinkles in adults. LAVIV utilizes our proprietary autologous fibroblast technology. In 2013, we shifted our strategic focus away from the aesthetic market and towards developing treatments for diseases affecting the skin, connective tissue and joints. As a result, we no longer actively market or promote LAVIV but we continue to accept prescriptions, from which we expect a nominal amount of revenue during 2016.

A condition to the FDA's approval of LAVIV was that we conduct a 2,700 patient post-marketing study by the end of 2016 to assess the risk of skin cancer (such as basal cell cancer) in the area of LAVIV injections and the risk of immune-mediated hypersensitivity reactions (such as leukocytoclastic vasculitis). We have initiated enrollment in this study and have submitted the required biannual interim reports to the FDA, with the most recent being in January 2016. However, given the limited use of LAVIV, we have experienced difficulties in recruiting a sufficient number of patients for this study. We are actively engaged in discussions with the FDA about how to fulfill the study size requirement in light of the limited population of LAVIV users.

Intrexon Collaborations

2012 Exclusive Channel Collaboration Agreement ("2012 ECC")

In October 2012, we entered into an Exclusive Channel Collaboration Agreement, with Intrexon, which was amended in June 2013 and January 2014 (as amended, the "2012 ECC") pursuant to which we are Intrexon's exclusive channel collaborator in the research, development and commercialization of products in the following areas (the "2012 Fields"):

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the enhanced production and purification of autologous fibroblasts (without genetic modification) for all aesthetic and therapeutic indications;

- the enhanced production and purification of autologous dermal cells (without genetic modification) for aesthetic and therapeutic treatment of dermal, vocal cord, and periodontal indications;
- the development of genetically modified autologous fibroblasts for all aesthetic and therapeutic indications where an autologous fibroblast itself is the principal effector of the product in contrast to the use of autologous fibroblasts as the source of expression of a systemically available therapeutic protein in which that protein (and not the fibroblast) is the principal therapeutic effector;

Table of Contents

- the development of genetically modified autologous dermal cells for aesthetic and therapeutic treatment of dermal, vocal cord, and periodontal indications;
- autologous fibroblasts genetically modified to express a therapeutic protein and/or bioactive ribonucleic acid for the treatment of autoimmune and non-infectious inflammatory disorders that manifest in cutaneous tissues, fascia and/or muscle; and
- autologous human fibroblasts with gene therapy to express bioactive Tenascin-X locally to correct connective tissue disorders associated with Ehlers-Danlos Syndrome (hypermobility type).

Pursuant to the terms of the 2012 ECC, Intrexon has granted us a license to use its proprietary technologies and other intellectual property to research, develop and commercialize products in the 2012 Fields within the United States. We are responsible for all costs incurred in connection with the research, development and commercialization of products under the 2012 ECC and own all clinical data, regulatory filings and regulatory approvals relating to such products. We engage Intrexon for support services for the research and development of products under the 2012 ECC, and reimburse Intrexon for its cost for time and materials for such services.

We are required to pay Intrexon quarterly cash royalties on all products developed under the 2012 ECC in an amount equal to 7% of aggregate annualized net sales up to $100 million, plus 14% on aggregate annualized net sales greater than $100 million. We are also required to pay Intrexon half of any sublicensing revenues we receive from third parties in consideration for sublicenses granted by us with respect to products developed under the 2012 ECC, but only to the extent such sublicensing revenues are not included in net sales subject to royalties. Sales from LAVIV (azficel-T), including new indications, or other products that we develop and commercialize outside of the 2012 ECC are not subject to royalty payments unless we are able to reduce the product's cost of goods sold through the 2012 ECC, in which case, we are required to pay quarterly cash royalties on such products equal to one-third of the cost of goods sold savings less any such savings developed by us outside of the 2012 ECC.

The 2012 ECC may be terminated by Intrexon if we fail to exercise diligent efforts in developing products through the collaboration or if we elect not to pursue the development of a therapy identified by Intrexon within the 2012 Field and that qualifies as a “Superior Therapy” as defined in the 2012 ECC. Upon such termination, the products covered by the 2012 ECC in active and ongoing Phase II clinical trials or later stage development shall be entitled to be continued by us with a continuation of the related milestone, royalty and other payment obligations for such products, and all rights to products covered by the 2012 ECC still in an earlier stage of development shall revert to Intrexon.

In September 2015, we and Intrexon entered into a letter of agreement pursuant to which we mutually agreed to terminate our collaboration with respect to the development of potential therapies to treat Ehlers-Danlos Syndrome (hypermobility type) due to technical hurdles. As a result, we no longer have any rights or obligations under the 2012 ECC with respect to the development of “autologous human fibroblasts genetically modified to express bioactive Tenascin-X locally to correct connective tissue disorders”.

Currently, we are in pre-clinical development of two gene-therapy product candidates, FCX-007 and FCX-013, under the 2012 ECC.

2015 Exclusive Channel Collaboration Agreement ("2015 ECC")

In December 2015, we entered into an additional Exclusive Channel Collaboration Agreement with Intrexon (the "2015 ECC") pursuant to which we are Intrexon's exclusive channel collaborator in the research, development and commercialization of products for the treatment of chronic inflammation and degenerative diseases of human joints through intra-articular or other local administration of genetically-modified fibroblasts (the "2015 Field"). The collaboration leverages our autologous fibroblast technology with Intrexon's synthetic biology technology to identify and develop cell-based therapeutics that will be genetically modified to express one or more proteins at sites of joint

inflammation. We believe this treatment approach has the potential to overcome the limitations of existing therapies for chronic inflammation and degenerative diseases of the joint, including arthritis and related conditions.

Pursuant to the terms of the 2015 ECC, Intrexon has granted us a license to use its proprietary technologies and other intellectual property to develop and commercialize products in the 2015 Field throughout the world. We are responsible for all costs incurred in connection with the research, development and commercialization of products under the 2015 ECC and own all clinical data, regulatory filings and regulatory approvals relating to such products. We engage Intrexon for support services in connection with the research and development of products under the 2015 ECC, and reimburse Intrexon for its cost for time and materials for such services.

Table of Contents

For each product that we develop under the 2015 ECC, we are required to pay Intrexon development milestones of up to $30 million and commercialization milestones of up to $22.5 million, a low double-digit royalty on our net sales of such products and half of any sublicensing revenues we receive from third parties in consideration for sublicenses granted by us with respect to such products but only to the extent such sublicensing revenues are not included in net sales subject to royalties.

The 2015 ECC may be terminated by Intrexon if we fail to exercise diligent efforts in developing products through the collaboration or if we elect not to pursue the development of a therapy identified by Intrexon within the 2015 Field and that qualifies as a “Superior Therapy” as defined in the 2015 ECC. Upon such termination, the products covered by the 2015 ECC in active and ongoing Phase II clinical trials or later stage development shall be entitled to be continued by us with a continuation of the related milestone, royalty and other payment obligations for such products, and all rights to products covered by the 2015 ECC still in an earlier stage of development shall revert to Intrexon.

Currently, we are in the research phase for a gene-therapy product for arthritis under the 2015 ECC.

UCLA Collaboration

In May 2014, we entered into a research agreement with The Regents of the University of California ("UCLA") pursuant to which we and UCLA agreed to undertake collaborative research activities over a three to five year period to develop novel intellectual property and products relating to (a) somatic dermal derivatives and (b) human induced pluripotent stem cells. In connection with this collaboration, we and UCLA also entered into an exclusive license agreement in June 2014 pursuant to which UCLA granted us an exclusive, sublicensable right and license to use certain intellectual property developed under this program for all research, development and commercialization purposes. In consideration for the license, we are required to pay to UCLA a license issue fee, a license maintenance fee (waived if earned royalties are paid), certain one-time milestone payments, earned royalties on net sales of licensed products (including sales by affiliates) and a percentage of amounts received from sublicensing activities. We are also subject to minimum annual royalty payments to UCLA beginning after the first commercial sale of a licensed product.

We had previously been a party to additional collaborations with UCLA relating to isolating stem cell sub-populations in the skin; however, we terminated these programs and related agreements during 2015.

Manufacturing

We lease and operate our own manufacturing facility located in Exton, Pennsylvania. We use this facility to manufacture our non-genetically modified products. We outsource the manufacturing for our genetically-modified product candidates to a contract manufacturer with a facility located in Mountain View, California. We and our contract manufacturer are subject to routine inspections in accordance with the FDA's Current Good Manufacturing Practices (“cGMP”). We believe that we and our contract manufacturer have adequate manufacturing capacity to satisfy our clinical demands, as well as the limited commercial demand we expect during 2016.

The fibroblast cells that constitute our product candidates are grown by our proprietary manufacturing process which begins with the collection of skin biopsies from behind the ear on the patient’s skin. The biopsies are then sent to us for processing according to cGMP and, for our genetically-modified product candidates, cell engineering. The cells are then expanded using tissue culture techniques and cryo-preserved. When a treatment is requested, the cells are further processed and prepared for shipment.

All component parts, including raw materials and other supplies utilized in our manufacturing process are available from various third party suppliers and manufacturers in quantities adequate to meet our needs. We seek to ensure continuity of supply of such component parts, raw materials and supplies using a strategy of dual sourcing, where

possible. Some of our raw materials are currently sourced from one vendor; however, alternate vendors are available should they be required, although we would need sufficient lead time to qualify those vendors.

We use certain hazardous chemicals and biological materials in our manufacturing process which are subject to a variety of federal, state and local laws and regulations governing, among other matters, the use, generation, manufacture, transportation, storage, handling, disposal of and human exposure to these materials, including regulation by governmental regulatory agencies, such as the Occupational Safety and Health Administration and the U.S. Environmental Protection Agency. We incur capital and operating expenditures and other costs in the ordinary course of our business in complying with these laws and regulations. We dispose of minimal hazardous biological waste as a result of our manufacturing process.

Table of Contents

Intellectual Property

We believe that patents, trademarks, copyrights and other proprietary rights are important to our business. We also rely on trade secrets, know-how and continuing technological innovations to develop and maintain our competitive position. We seek to protect our intellectual property rights by a variety of means, including obtaining patents, maintaining trade secrets and proprietary know-how and technological innovation to operate, without infringing on the proprietary rights of others and to prevent others from infringing on our proprietary rights.

As of December 31, 2015, we own or license 11 issued U.S. patents, 9 pending U.S. patent applications, 10 granted foreign patents, 1 pending international patent and 14 pending foreign patent applications. Our issued patents and patent applications primarily cover the method of using autologous cell fibroblasts for the repair of skin and soft tissue defects and the use of autologous fibroblast cells for tissue regeneration. In particular, we own issued patents in the U.S. and in other countries that are directed to methods of long-term augmentation of subcutaneous or dermal tissue by injecting an effective amount of a suspension of autologous passaged dermal fibroblasts into subadjacent tissue, which covers the approved use of LAVIV, as well as azficel-T for the treatments of vocal cord scarring and restrictive burn scarring, and which are set to expire in the U.S. in July 2020. In addition, we own an issued U.S. patent and pending applications in Australia, Canada, China, Europe, India, Japan, South Korea, Hong Kong and the U.S. directed to dosage formulations for injection containing particular amounts of autologous human fibroblasts and uses thereof, which also covers LAVIV as well as azficel-T for the treatments of vocal cord and restrictive burn scarring, and which naturally expire in 2030 and 2031. We also own pending applications in the U.S. and several foreign countries related to topical formulations of autologous dermal fibroblasts and uses thereof, the earliest of which, if issued, would naturally expire in 2027.

Competition

There is significant competition in the biopharmaceutical industry which can be attributed to companies ranging from small specialized biotechnology firms to large well-established pharmaceutical companies. More specifically, there are many companies currently competing in drug development for new therapies for the treatment of diseases affecting the skin, connective tissue and joints, our focus area. Some of our competitors have substantially greater financial resources and larger research and development organizations. In addition, our experience in clinical trials, obtaining FDA and other regulatory approvals, manufacturing and commercialization of products may be more limited.

Product competition is based on a variety of factors, including but not limited to: product safety, efficacy, convenience of dosing, availability, price, as well as brand recognition. Our product candidates, if approved for commercial use, will contend with treatments offered by our competitors. Although we believe the autologous nature and localized treatment approach of our product candidates provide advantages over our competitors, existing and new treatments may also possess certain advantages. Additionally, the development of other drug technologies and methods of treating diseases are occurring at a rapid pace. These developments may render our products or technologies obsolete or noncompetitive. Currently, we believe the primary competitors for our product candidates are as follows:

azficel-T for Vocal Cord Scarring. Our product candidate azficel-T is being developed to treat vocal cord scarring resulting in chronic or severe dysphonia. Current treatments for vocal cord scarring, which include voice therapy and surgery through the use of injection (collagen, fat, calcium, hyaluronic acid) or implant (PTFE, silastic), only address the symptoms of this condition. PROLARYN™ (injectable implant) is currently marketed by Merz North America, Inc. as a treatment for dysphonia and vocal cord insufficiency.

FCX-007 for RDEB. Our product candidate FCX-007 is being developed for the treatment of RDEB. Current treatments for RDEB, which include bandaging, antibiotics, feeding tubes, and surgery (hand and esophageal), only address the symptoms of this disorder. There are currently no products approved by the FDA for the treatment of

RDEB. We are aware of a potentially competing product, ZORBLISA™ (SD-101 Cream), which is being developed by Amicus Therapeutics and is in a Phase III trial for the treatment of epidermolysis bullosa.

FCX-013 for Linear Scleroderma. Our product candidate FCX-013 is being developed for the treatment of linear scleroderma. Current treatments for linear scleroderma, which include systemic or topical corticosteroids, UVA light therapy, and physical therapy, only address the symptoms of the disorder. There are currently no products approved by the FDA for the treatment of linear scleroderma. We are aware of a potentially competing product, ECCS-50 Cellular Therapy, which is being developed by Cytori Therapeutics and is in a Phase III clinical trial for the treatment of scleroderma that affects the hands. We are also aware that miRagen Therapeutics has a product candidate utilizing microRNA biology in a Phase I clinical trial for the treatment of systemic and localized scleroderma.

Table of Contents

Research and Development

We expense research and development costs as they are incurred. For the years ended December 31, 2015, 2014 and 2013, we incurred total research and development expenses of $25.9 million, $17.7 million and $13.8 million, respectively. Additionally, for the year ended December 31, 2015, we incurred expenses of $0.3 million related to a research and development agreement that the Company has with a third party to investigate potential new non-pharmaceutical applications for the Company's conditioned fibroblast media technology. Expenses pertaining to this collaboration agreement are classified under the caption "Cost of collaboration revenue" in the Consolidated Statements of Operations. No such expenses were incurred during the years ended December 31, 2014 or 2013.

Government Regulation

We are subject to extensive government regulation, principally by the FDA and state and local authorities in the United States and by comparable agencies in foreign countries. Governmental authorities in the United States extensively regulate the pre-clinical and clinical testing, safety, efficacy, research, development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution, among other things, of pharmaceutical and biologic products under various federal laws including the Federal Food, Drug and Cosmetic Act ("FFDCA"), the Public Health Service Act ("PHSA") and under comparable laws by the states and in most foreign countries.

Domestic Regulation

In the United States, the FDA, under the FFDCA, the PHSA, and other federal statutes and regulations, subjects pharmaceutical and biologic products to rigorous review. If we do not comply with applicable requirements, we may be fined, the government may refuse to approve our marketing applications or allow us to manufacture or market our products or product candidates, and we may be criminally prosecuted. The FDA also has the authority to discontinue or suspend manufacture or distribution, require a product withdrawal or recall or revoke previously granted marketing authorizations if we fail to comply with regulatory standards or if we encounter problems during commercial operations.

FDA Approval Process

To obtain approval of a new product from the FDA, we must, among other requirements, submit data demonstrating the product’s safety and efficacy as well as detailed information on the manufacture and composition of the product candidate. In most cases, this entails extensive laboratory tests and pre-clinical and clinical trials. This testing and the preparation of necessary applications and processing of those applications by the FDA are expensive and typically take many years to complete. The FDA may deny our applications or may not act quickly or favorably in reviewing these applications, and we may encounter significant difficulties or costs in our efforts to obtain FDA approvals that could delay or preclude us from marketing any products we may develop. The FDA also may require post-marketing testing and surveillance to monitor the effects of approved products or place conditions on any approvals that could restrict the commercial applications of these products. Regulatory authorities may withdraw product approvals if we fail to comply with regulatory standards or if we encounter problems following initial marketing. With respect to patented products or technologies, delays imposed by the governmental approval process may materially reduce the period during which we may have the exclusive right to exploit the products or technologies.

The FDA does not apply a single regulatory scheme to human tissues and the products derived from human tissue. On a product-by-product basis, the FDA may regulate products as drugs, biologics, or medical devices, in addition to regulating them as human cells, tissues, or cellular or tissue-based products (“HCT/P”), depending on whether or not the particular product triggers any of an enumerated list of regulatory factors. A fundamental difference in the treatment of products under these classifications is that the FDA generally permits HCT/Ps that do not trigger any of those

regulatory factors to be commercially distributed without regulatory approval. In contrast, products that trigger those factors, such as if they are more than minimally manipulated when processed or manufactured, are regulated as drugs, biologics, or medical devices and require FDA approval. We have determined that LAVIV and our product candidates trigger regulatory factors that make them biologics, in addition to an HCT/P, and consequently, we must obtain approval from the FDA before marketing such products and must also satisfy all regulatory requirements for HCT/Ps.

The process required by the FDA before a new drug or biologic may be marketed in the United States generally involves the following:

- completion of pre-clinical laboratory tests or studies and formulation studies;

Table of Contents

- submission to the FDA of an IND application for a new drug or biologic, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug or biologic for its intended use;
- detailed information on product characterization and manufacturing process; and
- submission and approval of a New Drug Application ("NDA") for a drug, or a BLA for a biologic.

Pre-clinical tests include laboratory evaluation of product chemistry formulation and stability, as well as animal and other studies to evaluate toxicity. Under FDA regulations, the results of any pre-clinical testing, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application. The FDA requires a 30-day waiting period after the filing of each IND application before clinical trials may begin, in order to ensure that human research patients will not be exposed to unreasonable health risks. At any time during this 30-day period or at any time thereafter, the FDA may halt proposed or ongoing clinical trials, may authorize trials only on specified terms, or may require additional trials. The IND application process may become extremely costly and substantially delay development of our products. Moreover, positive results of pre-clinical tests will not necessarily indicate positive results in clinical trials.

The sponsor typically conducts human clinical trials in three sequential phases, which may overlap. These phases generally include the following:

- Phase I: The product candidate is usually first introduced into healthy humans or, on occasion, into patients, and is tested for safety, dosage tolerance, absorption, distribution, excretion and metabolism;
- Phase II: The product candidate is introduced into a limited patient population to:
  - assess its efficacy in specific, targeted indications;
  - assess dosage tolerance and optimal dosage; and
  - identify possible adverse effects and safety risks.
- Phase III: These are commonly referred to as pivotal studies. If a product candidate is found to have an acceptable safety profile and to be potentially effective in Phase II clinical trials, clinical trials in Phase III will be initiated to further demonstrate clinical efficacy, optimal dosage and safety within an expanded and diverse patient population at geographically dispersed clinical trial sites; and
- If the FDA does ultimately approve the product candidate, it may require post-marketing testing, including potentially expensive Phase IV studies, to confirm or further evaluate its safety and effectiveness. Continued ability to commercialize the product may be based on the successful completion of these additional studies.

Before proceeding with a trial, the sponsor may seek a written agreement from the FDA regarding the design, size, and conduct of a clinical trial. This is known as a Special Protocol Assessment ("SPA"). Among other things, SPAs can cover clinical trials for pivotal studies whose data will form the primary basis to establish a product's efficacy. SPAs thus help establish up-front agreement with the FDA about the adequacy of a clinical trial design to support a regulatory approval, but the agreement is not binding if new circumstances arise. Even if the FDA agrees to a SPA, the agreement may be changed by the sponsor or the FDA on written agreement by either parties, or if a senior FDA official determines that a substantial scientific issue essential to determining the safety or effectiveness of the product was identified after the testing began. There is no guarantee that a study will ultimately be adequate to support an approval, even if the study is subject to a SPA. The FDA retains significant latitude and discretion in interpreting the terms of the SPA and the data and results from any study that is the subject of the SPA.

Clinical trials must meet requirements for Institutional Review Board ("IRB") oversight, patient informed consent and the FDA's Good Clinical Practice ("GCP"). Prior to commencement of each clinical trial, the sponsor must submit to the FDA a clinical plan, or protocol, accompanied by the approval of the committee responsible for overseeing clinical trials at the clinical trial sites. The FDA or the IRB at each institution at which a clinical trial is being performed may order the temporary or permanent discontinuation of a clinical trial at any time if it believes that the clinical trial is not

being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. Data safety monitoring committees, which monitor certain studies to protect the welfare of study patients, may also require that a clinical trial be discontinued or modified.

Table of Contents

The sponsor must submit to the FDA the results of the pre-clinical and clinical trials, together with, among other things, detailed information on the manufacturing and composition of the product, and proposed labeling, in the form of an NDA, or, in the case of a biologic, a BLA. The applicant must also submit with the NDA or BLA a substantial user fee payment, unless a waiver or reduction applies. In some cases, a sponsor may be able to expand the indications in an approved NDA or BLA through a submission of a Prior Approval Supplement. Each NDA or BLA submitted for FDA approval is usually reviewed for administrative completeness and reviewability within 60 days following submission of the application. If deemed complete, the FDA will "file" the NDA or BLA, thereby triggering substantive review of the application. The FDA can refuse to file any NDA or BLA that it deems incomplete or not properly reviewable. Once the submission has been accepted for filing, the FDA will review the application and will usually respond to the applicant in accordance with performance goals the FDA has established for the review of NDAs and BLAs - six months from the receipt of the application for priority applications and ten to twelve months for regular applications. The review process is often significantly extended by FDA requests for additional information, pre-clinical studies or clinical trials, clarification, or a risk evaluation and mitigation strategy ("REMS") or by changes to the application submitted by the applicant in the form of amendments. The FDA may refer applications for novel product candidates which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation, and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA or BLA, the FDA will often inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facilities are in compliance with cGMP requirements which govern the manufacture, holding and distribution of a product. Manufacturers of human cellular or tissue-based biologics also must comply with the FDA's Good Tissue Practices, as applicable, and the general biological product standards.

It is possible that our product candidates will not successfully proceed through this approval process or that the FDA will not approve them in any specific period of time, or at all. The FDA may deny or delay approval of applications that do not meet applicable regulatory criteria, or if the FDA determines that the clinical data does not adequately establish the safety and efficacy of the product. Satisfaction of FDA pre-market approval requirements for a new biologic is a process that may take a number of years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease. The FDA reviews these applications and, when and if it decides that adequate data is available to show that the product is both safe and effective and that other applicable requirements have been met, approves the drug or biologic for marketing. Government regulation may delay or prevent marketing of potential products for a considerable period of time and imposes costly procedures upon our activities. Success in early stage clinical trials does not assure success in later stage clinical trials. Data obtained from clinical activities is not always conclusive and may be susceptible to varying interpretations that could delay, limit or prevent regulatory approval. Upon approval, a product candidate may be marketed only for those indications approved in the NDA or BLA and will be subject to labeling and promotional requirements or limitations, including warnings, precautions, contraindications and use limitations, which could materially impact profitability. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-market regulatory standards and requirements are not maintained or if safety, efficacy or other problems occur after the product reaches the marketplace.

The FDA may, during its review of an NDA or BLA, ask for additional study data. If the FDA does ultimately approve the product, approval may be subject to limitations based on the FDA's interpretation of the existing pre-clinical and clinical data and the FDA may require post-marketing testing, including potentially expensive Phase IV studies, to confirm or otherwise further evaluate the safety and effectiveness of the product. The FDA also may require, as a condition to approval or continued marketing of a drug, a REMS to ensure that the benefits of a drug or biologic product outweigh its risks. REMS can include additional educational materials for healthcare professionals

and patients such as Medication Guides and Patient Package Inserts, a plan for communicating information to healthcare professionals, and restricted distribution of the product. In addition, the FDA may, in some circumstances, impose restrictions on the use of the product, which may be difficult and expensive to administer and may require prior approval of promotional materials. Following approval, the FDA may require labeling changes or impose new post-approval study, risk management, or distribution restriction requirements.

The FDA has developed four distinct approaches intended to make drugs that address unmet medical needs for serious or life threatening conditions available as rapidly as possible, especially when the drugs are the first available treatment or have advantages over existing treatments: accelerated approval, fast track, breakthrough therapy, and priority review.

- Accelerated Approval. The FDA may grant “accelerated approval” status to drugs or biologics that treat serious or life-threatening illnesses and that provide meaningful therapeutic benefits to patients over existing treatments. Under this pathway, the FDA may approve a product based on surrogate endpoints, or clinical endpoints other than survival or irreversible morbidity. When approval is based on surrogate endpoints or clinical endpoints other than survival or morbidity, the sponsor will be required to conduct additional post-approval clinical trials to verify and describe clinical benefit. Under the agency's accelerated approval regulations, if the FDA concludes that a

Table of Contents

product that has been shown to be effective can be safely used only if distribution or use is restricted, it may require certain post-marketing restrictions as necessary to assure safe use. In addition, for products approved under accelerated approval, sponsors will be required to submit all copies of their promotional materials, including advertisements, to the FDA at least thirty days prior to initial dissemination unless otherwise informed by the FDA. After a hearing, the FDA may withdraw a previously granted accelerated approval if, for instance, post-marketing studies fail to verify any clinical benefit, it becomes clear that restrictions on the distribution of the product are inadequate to ensure its safe use, or if a sponsor fails to comply with the conditions of the accelerated approval.

- Breakthrough Therapy. The FDA may grant “breakthrough therapy” status to drugs or biologics designed to treat, alone or in combination with another drug(s) or biologic(s), a serious or life-threatening disease or condition and for which preliminary evidence suggests a substantial improvement on clinically-meaningful endpoints over existing therapies. Such products need not address an unmet need, but are nevertheless eligible for expedited review if they offer the potential for an improvement over existing therapies. Breakthrough therapy status entitles the sponsor to earlier and more frequent meetings with the FDA regarding the development of nonclinical and clinical data and permits the FDA to offer product development or regulatory advice for the purpose of shortening the potential time to product approval. Breakthrough therapy status does not guarantee that a product will be developed or reviewed more quickly and does not ensure FDA approval.
- Fast Track. The FDA may grant “fast track” status to drugs or biologics that treat serious diseases or illness and fill an unmet medical need. Fast track is a process designed to expedite the review of such products by providing, among other things, more frequent meetings with the FDA to discuss the product's development plan, more frequent written correspondence from the FDA about trial design, eligibility for accelerated approval, and rolling review, which allows submission of individually completed sections of a NDA or BLA for the FDA's review before the entire filing is completed. Fast track status does not ensure that a product will be developed more quickly or receive FDA approval more quickly, if at all.
- Priority Review. The FDA may grant “priority review” status to products that, if approved, would be significant improvements in safety or effectiveness of the treatment, diagnosis or prevention of serious conditions. Priority review is intended to reduce the time it takes for the FDA to review a NDA or BLA.

Additionally, there are various designations available to drugs and biologics which provide a sponsor with incentives to support approval of the product candidate, including, but is not limited to, orphan drug designation and rare pediatric disease designation.

Orphan Drug Designation

Under the U.S. Orphan Drug Act, the FDA may grant orphan drug designation to drugs or biologics intended to treat a "rare disease or condition," which is defined as having a prevalence of less than 200,000 individuals in the U.S. Orphan drug designation must be requested before submitting a NDA or BLA for the product. Orphan drug designation does not shorten the regulatory review and approval process, nor does it provide any advantage in the regulatory review and approval process. However, if an orphan drug later receives approval for the indication for which it has designation, the relevant regulatory authority may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years in the U.S. Although obtaining approval to market a product with orphan drug exclusivity may be advantageous, we cannot be certain:

- that we will be the first to obtain approval for any drug for which we obtain orphan drug designation;
- that orphan drug designation will result in any commercial advantage or reduce competition; or
- that the limited exceptions to this exclusivity will not be invoked by the relevant regulatory authority.

Additionally, orphan drug exclusive marketing rights may be lost under certain conditions, such as if the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug.

FCX-007 has received orphan drug designation from the FDA and we plan to seek orphan drug designation for FCX-013.

Table of Contents

Rare Pediatric Disease Designation

FCX-007 has received rare pediatric disease designation from the FDA for the treatment of RDEB. The FDA defines a "rare pediatric disease" as a disease that affects fewer than 200,000 individuals in the U.S. primarily under the age of 18 years old. Under the FDA's Rare Pediatric Disease Priority Review Voucher program, upon the approval of a NDA or BLA of a product for the treatment of a rare pediatric disease, the sponsor of such application is eligible for a Rare Pediatric Disease Priority Review Voucher. Currently, the Priority Review Voucher can be used to obtain priority review for any subsequent NDA or BLA and may be sold or transferred an unlimited number of times. Congress has extended the Priority Review Voucher Program until September 30, 2016. Because this program has been subject to criticism, including by the FDA, it is possible that even if we obtain approval for FCX-007 and qualify for a Priority Review Voucher, the program may no longer be in effect at the time of FCX-007's approval.

Ongoing FDA Requirements and Post-Marketing Obligations

The Food and Drug Administration Amendments Act of 2007 expanded FDA authority over drug products after approval. All approved drug products are subject to continuing regulation by the FDA, including record-keeping requirements, reporting of adverse experiences with the product, sampling and distribution requirements, notifying the FDA and gaining its approval of certain manufacturing or labeling changes, complying with certain electronic records and signature requirements, submitting periodic reports to the FDA, maintaining and providing updated safety and efficacy information to the FDA, and complying with FDA promotion and advertising requirements. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, seizure of product, injunctive action, criminal prosecution, or civil penalties.

The FDA may require post-marketing studies or clinical trials to develop additional information regarding the safety of a product. These studies or trials may involve continued testing of a product and development of data, including clinical data, about the product’s effects in various populations and any side effects associated with long-term use. The FDA may require post-marketing studies or trials to investigate possible or known serious risks or signals of serious risks, or to identify unexpected serious risks, and may require periodic status reports if new safety information develops. Failure to conduct these studies in a timely manner may result in substantial civil fines, or withdrawal of product approval.

A condition to the FDA's approval of LAVIV was that we conduct a 2,700 patient post-marketing study by the end of 2016 to assess the risk of skin cancer (such as basal cell cancer) in the area of LAVIV injections and the risk of immune-mediated hypersensitivity reactions (such as leukocytoclastic vasculitis). We have initiated enrollment in this study and have submitted the required biannual interim reports to the FDA, with the most recent being in January 2016. However, given the limited use of LAVIV, we have experienced difficulties in recruiting a sufficient number of patients for this study. We are actively engaged in discussions with the FDA about how to fulfill the study size requirement in light of the limited population of LAVIV users.

Also, newly discovered or developed safety or efficacy data may require changes to a product’s approved labeling, including the addition of new warnings and contraindications, additional pre-clinical studies or clinical trials, or even in some instances, withdrawal of the approval. Violations of regulatory requirements at any stage, including after approval, may result in various adverse consequences, including the FDA’s withdrawal of an approved product from the market, other voluntary or FDA-initiated action that could delay or restrict further marketing, and the imposition of civil fines and criminal penalties against the manufacturer and NDA or BLA holder. In addition, later discovery of previously unknown problems may result in restrictions on the product, manufacturer or NDA or BLA holder, including withdrawal of the product from the market.

The labeling, advertising, promotion, marketing and distribution of a drug or biologic product also must be in compliance with FDA and Federal Trade Commission ("FTC") requirements which include, among others, promotional activities, standards and regulations for direct-to-consumer advertising, promotional activities involving the internet, and industry sponsored scientific and educational activities. In general, all product promotion must be consistent with the labeling approved by the FDA for such product, contain a balanced presentation of information on the product's uses, benefits, risks, and important safety information and limitations on use, and otherwise not be false or misleading. The FDA, as well as the FTC, have very broad enforcement authority, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing a company to correct deviations from regulatory standards and enforcement actions that can include seizures, injunctions and criminal prosecution. Failure to comply with applicable FDA requirements and restrictions also may subject a company to adverse publicity and enforcement action by the FDA, the U.S. Department of Justice ("DOJ") or the Office of the Inspector General of the U.S. Department of Health and Human Services ("HHS") as well as state authorities. This could subject the company to a range of penalties that could have a significant commercial impact, including

Table of Contents

civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes its products.

Drug and biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and to list their products with the FDA. The FDA periodically inspects manufacturing facilities in the United States and abroad in order to assure compliance with the applicable cGMP regulations and other requirements. Facilities also are subject to inspections by other federal, foreign, state or local agencies. In complying with the cGMP regulations, manufacturers must continue to assure that the product meets applicable specifications, regulations and other post-marketing requirements. Failure to comply with these requirements subjects the manufacturer to possible legal or regulatory action, such as suspension of manufacturing or recall or seizure of product.

Sponsors and their third-party contractors are also subject to various laws and regulations governing laboratory practices, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances in connection with their research. In each of the above areas, the FDA has broad regulatory and enforcement powers, including the ability to levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products and deny or withdraw approvals.

Furthermore, new government requirements may be established that could delay or prevent regulatory approval of our products under development, or affect the conditions under which approved products are marketed.

HIPAA Requirements

Other federal legislation may affect our ability to obtain certain health information in conjunction with our research activities. We may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. The Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (“HITECH”), and its implementing regulations, imposes requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA’s privacy and security standards directly applicable to “business associates”— independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney’s fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Other U.S. Regulatory Requirements

In the United States, the research, manufacturing, distribution, sale, and promotion of drug and biologic products are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services (formerly the Health Care Financing Administration), other divisions of the HHS (e.g., the Office of Inspector General), the DOJ and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, sales, marketing and scientific/educational grant programs must comply with the anti-fraud and abuse provisions of the Social Security Act, the False Claims Act, and similar state laws, each as amended.

If a drug or biologic product is reimbursed by Medicare or Medicaid, pricing and rebate programs must comply with, as applicable, the Medicare Modernization Act as well as the Medicaid rebate requirements of the Omnibus Budget

Reconciliation Act of 1990 (“OBRA”) and the Veterans Health Care Act of 1992 (“VHCA”), each as amended. Among other things, the OBRA requires pharmaceutical manufacturers to pay rebates on prescription products to state Medicaid programs and empowers states to negotiate rebates on pharmaceutical prices, which may result in prices for our future products that will likely be lower than the prices we might otherwise obtain. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Under the VHCA, drug companies are required to offer some products at a reduced price to a number of federal agencies including the U.S. Department of Veterans Affairs and the U.S. Department of Defense, the Public Health Service and some private Public Health Service designated entities in order to participate in other federal funding programs including Medicaid. Participation under the VHCA requires submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulation. All of these activities are also potentially subject to federal and state consumer protection, unfair competition, and other laws.

Table of Contents

In March 2010, President Obama signed one of the most significant healthcare reform measures in decades. The Affordable Care Act, substantially changes the way healthcare will be financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. The Affordable Care Act was a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The Affordable Care Act has resulted in, and we expect it will continue to result in, downward pressure on coverage and the price of products covered by Medicare and other government programs. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments and coverage from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. In addition, it is possible that there will be further legislation or regulation that could harm our business, financial condition and results of operations.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting some business arrangements from prosecution, the exemptions and safe harbors are drawn narrowly and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from federal Anti-Kickback Statute liability. The reach of the Anti-Kickback Statute was broadened by the Affordable Care Act, which, among other things, amends the intent requirement of the federal Anti-Kickback Statute. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below) or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes “any request or demand” for money or property presented to the U.S. government. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies’ marketing of the product for unapproved, and thus non-reimbursable, uses. HIPAA created new federal criminal statutes that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

International Regulation

The regulation of our product candidates outside of the United States varies by country. Certain countries regulate human tissue products as a pharmaceutical product, which would require us to make extensive filings and obtain regulatory approvals before selling our product candidates. Certain other countries classify our product candidates as human tissue for transplantation but may restrict its import or sale. Other countries may have no application regulations regarding the import or sale of products similar to our product candidates, creating uncertainty as to what standards we may be required to meet.

Employees

As of December 31, 2015, we had 52 full-time employees, all located in the United States. Of these full-time employees, 39 are engaged in research, development and manufacturing (including facilities) functions and 13 are engaged in finance, legal, human resources, information technology, and other general administrative functions. None of our employees are covered by a collective bargaining agreement, and we consider our relations with our employees to be good.

Table of Contents

Corporate Information

We were incorporated under the laws of the State of Delaware in September 1992. Our corporate office is located at 405 Eagleview Boulevard, Exton, Pennsylvania 19341. Our telephone number is (484) 713-6000. We maintain an Internet website at www.fibrocell.com. The information contained on our website is not incorporated by reference into this Form 10-K.

We file reports, proxy and information statements and other information with the SEC. We make available free of charge under the “Investors—SEC Filings” section of our website all of our filings with the SEC, including our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, proxy statements and amendments to such documents, each of which is provided on our website as soon as reasonably practicable after we electronically file the information with the SEC.

The public may read and copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Additionally, the SEC maintains a website (www.sec.gov) that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including us.

Item 1A. Risk Factors

Our business is subject to substantial risks and uncertainties. The occurrence of any of the following risks and uncertainties, either alone or taken together, could materially and adversely affect our business, financial condition, results of operations or prospects. In these circumstances, the market price of our common stock could decline and you may lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Risks and uncertainties of general applicability and additional risks and uncertainties not currently known to us or that we currently deem to be immaterial may also materially and adversely affect our business, financial condition, results of operations or prospects.

Risks Related to our Financial Position and Need for Additional Capital

We need to obtain additional capital to continue as a going concern. If we are unable to obtain sufficient capital, we will need to curtail and reduce our operations and costs, and modify our business strategy.

Our principal sources of liquidity are cash and cash equivalents of $29.3 million as of December 31, 2015. As of December 31, 2015, we had working capital of $15.6 million. We believe that our existing cash and cash equivalents will be sufficient to fund our operations into the fourth quarter of 2016. However, changing circumstances may cause us to consume capital faster than we currently anticipate, and we may need to spend more money than currently expected because of such circumstances.

To meet our capital needs, we are considering multiple alternatives, including but not limited to, equity financings, debt financings, corporate collaborations, partnerships and other strategic transactions and funding opportunities. However, there can be no assurance that we will be able to complete any such transaction on acceptable terms or otherwise. These factors raise substantial doubt about our ability to continue as a going concern. As a result, our independent registered public accounting firm has included an explanatory paragraph in its report on our financial statements for the year ended December 31, 2015 related to our ability to continue as a going concern.

If we raise additional funds by issuing equity securities, our stockholders will experience dilution. Debt financing, if available, will result in increased fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Any debt financing or additional equity that we raise may contain terms, such as

liquidation and other preferences, which are not favorable to us or our stockholders. If we raise additional funds through collaboration or partnership arrangements with third parties, it may be necessary to relinquish valuable rights to our technologies, future revenue streams or product candidates or to grant licenses on terms that may not be favorable to us.

If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will need to curtail and reduce our operations and costs, and modify our business strategy which may require us to, among other things:

- significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates or one or more of our other research and development initiatives;
- seek collaborators for one or more of our current or future product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available;

Table of Contents

- sell or license on unfavorable terms our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves; or
- seek bankruptcy protection which may result in the termination of agreements pursuant to which we license important intellectual property rights including our exclusive collaboration agreements with Intrexon.

We have incurred significant losses since our inception and anticipate that we will continue to incur losses in the future.

We have incurred losses since our inception, have not generated significant revenue from commercial sales of our products, and have never been profitable. Since 2013, which is when we changed our business strategy to focus on therapeutic indications for azficel-T and on diseases affecting the skin and connective tissue in collaboration with our partner Intrexon, we have reduced sales and marketing efforts of LAVIV. We fulfilled a nominal amount of prescriptions for LAVIV aesthetic procedures in 2014 and 2015 and will continue to do so in 2016. Investment in drug development is highly speculative because it entails substantial upfront capital expenditures and significant risk that a product candidate will fail to gain regulatory approval or become commercially viable. We continue to incur significant research, development and other expenses related to our ongoing operations including development of our product candidates and operation of our manufacturing facility. As a result, we are not profitable and have incurred losses in each period since we emerged from bankruptcy in September 2009. For the year ended December 31, 2015, we reported a net loss of $34.5 million, and we had an accumulated deficit of $147.2 million at December 31, 2015.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will continue to be significant if and as we:

- continue our research and pre-clinical and clinical development of our product candidates;
- initiate additional pre-clinical, clinical or other studies or trials for our product candidates, including under our collaboration agreements with Intrexon;
- continue or expand our collaborations with Intrexon and our other collaborators;
- further develop the manufacturing process for our product candidates;
- continue to maintain a cGMP manufacturing facility;
- change or add additional manufacturers or suppliers;
- seek regulatory approvals for our product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain regulatory approval;
- seek to identify and validate additional product candidates;
- acquire or in-license other product candidates and technologies;
- maintain, protect and expand our intellectual property portfolio;
- attract and retain skilled personnel;
- create additional infrastructure to support our product development and planned future commercialization efforts; and
- experience any delays or encounter issues with any of the above.

The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

We do not generate significant revenues from product sales and may never be profitable.

Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory approvals necessary for, the manufacture and commercialization of our product candidates. Other than from the sale of LAVIV, we do not anticipate generating revenues from product sales for the foreseeable future, if ever. Our ability to generate future

revenues from product sales depends heavily on our success in:

Table of Contents

- completing research and pre-clinical and clinical development of our product candidates;
- seeking and obtaining regulatory approvals for product candidates for which we complete clinical trials;
- developing a sustainable, scalable, reproducible, and transferable manufacturing process for our product candidates;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate (in amount and quality) products and services to support clinical development and the market demand for our product candidates, if approved;
- launching and commercializing product candidates for which we obtain regulatory approval, either by collaborating with a partner or, if launched independently, by establishing a sales force, marketing, sales operations and distribution infrastructure;
- obtaining market acceptance of our product candidates and cell therapy and gene therapy as viable treatment options;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure, as needed;
- identifying and validating new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA or other regulatory agencies, domestic or foreign, to perform clinical trials or other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

We will seek to raise additional funds in the future, which may be dilutive to stockholders or impose operational restrictions.

We will need to raise additional capital in the future to help fund our clinical trials, our collaboration efforts with Intrexon and for the development and commercialization of our product candidates. If we raise additional capital through the issuance of equity securities, such as through our "at-the-market" equity program with Cantor Fitzgerald & Co., the percentage ownership of our current stockholders will be reduced. We may also issue equity as part of license issue fees to our licensors, compensate consultants or settle outstanding payables. Our stockholders may experience additional dilution in net book value per share and any additional equity securities may have rights, preferences and privileges senior to those of the holders of our common stock. Debt financing, if available, will result in increased fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Any debt financing or additional equity that we raise may contain terms, such as liquidation and other preferences, which are not favorable to us or our stockholders. If we raise additional funds through corporate collaboration, partnership or other strategic transactions, it may be necessary to relinquish valuable rights to our product candidates, our technologies or future revenue streams or to grant licenses or sell assets on terms that may not be favorable to us. If we cannot raise additional funds, we will have to delay our development activities or cease operations.

We have a limited operating history, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We have a limited operating history and our primary business activities consist of pre-clinical development and conducting clinical trials, pursuing our collaborations with Intrexon and commercializing LAVIV. As such, our historical financial data is of limited value in estimating future operating expenses. Our budgeted expense levels are based in part on our expectations concerning the costs of our pre-clinical development, clinical trials and our

collaborations with Intrexon, which depend on the success of such activities, and our ability to effectively and efficiently conduct such trials, pre-clinical development and our expectations related to our efforts to achieve FDA approval with respect to our product candidates. Our limited operating history and clinical trial experience make these costs difficult to forecast accurately. We may be unable to adjust our operations in a timely manner to compensate for any unexpected increase in costs. Further, our fixed manufacturing

Table of Contents

costs and operating expenses may increase significantly as we expand our operations. Accordingly, a significant increase in costs could have an immediate and material adverse effect on our business, results of operations and financial condition.

We may acquire other assets or businesses, or form collaborations or make investments in other companies or technologies that could harm our operating results, dilute our stockholders' ownership, incur debt or cause us to incur significant expense.

As part of our business strategy, we may pursue acquisitions of assets or businesses, or strategic alliances and collaborations, to expand our existing technologies and operations. We may not identify or complete these transactions in a timely manner, on a cost-effective basis, or at all, and we may not realize the anticipated benefits of any such transaction, any of which could have a detrimental effect on our financial condition, results of operations and cash flows. We may not be able to find suitable acquisition candidates, and if we make any acquisitions, we may not be able to integrate these acquisitions successfully into our existing business and we may incur debt or assume unknown or contingent liabilities in connection therewith. Integration of an acquired company or assets may also disrupt ongoing operations, require the hiring of additional personnel and the implementation of additional internal systems and infrastructure, especially the acquisition of commercial assets, and require management resources that would otherwise focus on developing our existing business. We may not be able to find suitable collaboration partners or identify other investment opportunities, and we may experience losses related to any such investments.

To finance any acquisitions or collaborations, we may choose to issue debt or shares of our common stock as consideration. Any such issuance of shares would dilute the ownership of our stockholders. If the price of our common stock is low or volatile, we may not be able to acquire other assets or companies or fund a transaction using our stock as consideration. Alternatively, it may be necessary for us to raise additional capital for acquisitions through public or private financings. Additional capital may not be available on terms that are favorable to us, or at all.

Risks Related to Clinical Development, Regulatory Approval and Commercialization of Our Product Candidates

Our gene-therapy product candidates are based on novel technology, which makes it difficult to predict the time and cost of product development and subsequently obtaining regulatory approval. At the moment, no gene therapy products have been approved in the United States and only one product has been approved in the European Union.

Our gene-therapy product candidates, including FCX-007 and FCX-013, are based on novel technology. Our future success depends on the successful development of this therapeutic approach. There can be no assurance that any development problems we experience in the future related to our gene-therapy product candidates will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays in developing a sustainable, reproducible and commercial-scale manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical studies or commercializing our gene-therapy products on a timely or profitable basis, if at all.

In addition, the clinical trial requirements of the FDA, the European Medicines Agency, or EMA, and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for gene-therapy product candidates such as ours can be more expensive and take longer than for other, better known or more extensively studied pharmaceutical or other product candidates. At the moment, only one gene-therapy product, UniQure's Glybera, which received marketing authorization in the European Union, or EU, in 2012, has been approved in the Western world, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our gene-therapy product candidates in the United States, the EU or other jurisdictions. Approvals by the EMA and the European Commission may not be indicative of what the FDA may require for approval.

Regulatory requirements governing gene and cell therapy products have evolved and may continue to change in the future. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the

Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health, or NIH, are also subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or RAC. Although the FDA decides whether individual gene therapy protocols may proceed, the RAC review process can impede the initiation of a clinical study, even if the FDA has reviewed the study and approved its initiation. Clinical trial sites in the United States that receive NIH funding for research involving recombinant or synthetic nucleic acid molecules are required to follow RAC recommendations, or risk losing NIH funding for such research or needing NIH pre-approval before conducting such research. In addition, the

Table of Contents

FDA can put an investigational new drug application, or IND, on clinical hold if the information in an IND is not sufficient to assess the risks in pediatric patients. Before a clinical study can begin at any institution, that institution's institutional review board, or IRB, and its Institutional Biosafety Committee will have to review the proposed clinical study to assess the safety of the trial. Moreover, serious adverse events or developments in clinical trials of gene therapy product candidates conducted by others may cause the FDA or other regulatory bodies to initiate a clinical hold on our clinical trials or otherwise change the requirements for approval of any of our product candidates.

These regulatory review agencies, committees and advisory groups and the new requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional or larger studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval studies, limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

The results seen in pre-clinical studies of our product candidates may not be replicated in humans.

Although we have seen positive results in pre-clinical studies of FCX-007 and FCX-013, we may not see positive results when these and any other product candidates undergo future clinical trials in humans. Pre-clinical studies are not
designed to test the efficacy of a product candidate in humans, but rather to:

- test short-term safety;
- establish biological plausibility;
- identify biologically active dose levels;
- establish feasibility and reasonable safety of the investigational product's proposed clinical route of administration;
- identify physiologic parameters that can guide clinical monitoring; and/or
- establish proof of concept, or the feasibility and rationale for use of an investigational product in the targeted patient population.

Success in pre-clinical studies does not ensure that later studies or any clinical trials will be successful nor does it predict future results. The rate of failure in drug development is quite high, and many companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in pre-clinical studies and earlier clinical trials. Product candidates may fail to show desired safety and efficacy when used with human patients. Negative or inconclusive results from any of our ongoing pre-clinical studies could result in delays, modifications, or abandonment of clinical trials and the termination of our development of a product candidate.

In September 2015, we received feedback from the FDA relating to our IND for FCX-007. If we are unable to adequately address the FDA's feedback, we will not be permitted to commence clinical trials of FCX-007, the development of FCX-007 will be further delayed and we will incur additional costs.

In September 2015, we received feedback from the FDA relating to our IND application for FCX-007, which required us to delay the initiation of our proposed Phase I/II clinical trial. The FDA's feedback related to the areas of CMC, toxicology and our proposed Phase I/II clinical trial protocol. Although the prior hybrid pharmacology/toxicology study performed based on the injection of FCX-007 into human skin that was xenografted onto SCID (severe combined immunodeficiency) mice was included in the IND and showed no signs of toxicity, the FDA requested that we execute an additional toxicology-specific study in which FCX-007 will be injected in non-grafted SCID mice. We

have initiated this new toxicology study, and we expect to amend the IND in response to the FDA's feedback and to include data from the new study in the first quarter of 2016. If we are unable to successfully complete the additional toxicology study and adequately address the FDA's other feedback, we will not be permitted to commence clinical trials, the development of FCX-007 will be further delayed and we will be required to incur additional costs in the development of FCX-007.

In previous clinical trials involving viral vectors for gene therapy, some patients experienced serious adverse events, including the development of leukemia due to vector-related insertional oncogenesis. If our vectors demonstrate a similar effect, we may be required to halt or delay further clinical development of our product candidates.

Table of Contents

A significant risk in any gene therapy product based on viral vectors is that the vector will insert in or near cancer-causing oncogenes leading to uncontrolled clonal proliferation of mature cancer cells in the patient. For example, in 2003, 20 patients treated for X-linked severe combined immunodeficiency in two gene therapy trials using a murine, or mouse-derived, gamma-retroviral vector showed correction of the disease, but the trials were terminated after five patients developed leukemia (four of whom were subsequently cured). The cause of these adverse events was shown to be insertional oncogenesis, which is the process whereby the corrected gene inserts in or near a gene that is important in a critical cellular process like growth or division, and this insertion results in the development of a cancer (often leukemia). Using molecular diagnostic techniques, it was determined that clones from these patients showed retrovirus insertion in proximity to the promoter of the LMO2 proto-oncogene. Earlier generation retroviruses like the one used in these two trials have been shown to preferentially integrate in regulatory regions of genes that control cell growth.

These well-publicized adverse events led to the development of new viral vectors, such as lentiviral vectors like the ones we utilize for FCX-007 and FCX-013, with potentially improved safety profiles and also the requirement of enhanced safety monitoring in gene therapy clinical trials, including periodic analyses of the therapy's genetic insertion sites. Notwithstanding the potential safety improvements of lentiviral vectors, the risk of insertional oncogenesis remains a significant concern for gene therapy and we cannot assure that it will not occur in any of our clinical trials. There is also the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. The FDA has stated that lentiviral vectors possess characteristics that may pose risks of delayed adverse events. If any such adverse events occur, further advancement of our clinical trials could be halted or delayed, which would have a material adverse effect on our business and operations.

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on the speed at which we can recruit patients to participate in testing our product candidates. We have experienced delays in some of our clinical trials, and we may experience similar delays in the future. If patients are unwilling to participate in our clinical trials because of negative publicity from adverse events in cell and gene therapies or for other reasons, including competitive clinical trials for similar patient populations, the timeline for recruiting patients, conducting clinical trials and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our technology or termination of the clinical trials altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a clinical trial or complete our clinical trials in a timely manner. Patient enrollment is affected by a variety factors including, among others:

- severity of the disease under investigation;
- design of the study protocol;
- prevalence of the disease/size of the patient population;
- eligibility criteria for the clinical trial in question;
- perceived risks and benefits of the product candidate under study;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

Our current product candidates are being developed to treat rare diseases with limited patient pools from which to draw for clinical trials and the process of finding and diagnosing patients may prove costly. We have estimated that there are approximately 1,100 to 2,500 U.S. patients with RDEB and approximately 40,000 U.S. patients with linear scleroderma over a major joint who exhibit severe joint pain. We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by the FDA or other regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business.

Table of Contents

Clinical trials may fail to demonstrate the safety or efficacy of our product candidates, which could prevent or significantly delay regulatory approval of our product candidates and harm our business.

Prior to receiving approval to commercialize any of our product candidates, we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA and other regulatory authorities in the United States and abroad, that our product candidates are both safe and effective. We will need to demonstrate our product candidates' efficacy and monitor their safety throughout the process. If our current or future clinical trials are unsuccessful, regulatory approval of our product candidates could be delayed or prevented and our business could be harmed.

All of our product candidates are subject to the risks of failure inherent in drug development. The results of early-stage clinical trials of our product candidates do not necessarily predict the results of later-stage clinical trials. Product candidates in later-stage clinical trials may fail to demonstrate desired safety and efficacy traits despite having successfully progressed through initial clinical testing. Even if we believe the data collected from clinical trials of our product candidates is promising, this data may not be sufficient to support approval by the FDA or any other U.S. or foreign regulatory approval. The FDA may also reject any of our completed clinical trials as inadequate to support approval if the study design does not include specific safety monitoring measures. Pre-clinical and clinical data can be interpreted in different ways. Accordingly, FDA officials could reach different conclusions in assessing such data than we do which could delay, limit or prevent regulatory approval. In addition, the FDA, other regulatory authorities, our IRB or we may suspend or terminate clinical trials at any time.

Obtaining FDA and other regulatory approvals is complex, time consuming and expensive, and the outcomes are uncertain.

The process of obtaining FDA and other regulatory approvals is time consuming, expensive and difficult. Clinical trials are required to establish the safety and efficacy of product candidates. Applications to market product candidates must be submitted to the FDA which must be reviewed for approval and approved by the FDA before product candidates may be marketed and clinical trials, manufacturing, and the marketing of products, if approved, are subject to strict regulatory compliance. The commencement and completion of clinical trials for any of our product candidates could be delayed or prevented by a variety of factors, including:

- delays in obtaining regulatory approvals to commence a study or trial;
- delays in identifying and reaching agreement on acceptable terms with prospective clinical trial sites;
- delays or failures in obtaining approval of our clinical trial protocol from an IRB to conduct a clinical trial at a prospective study site;
- delays in the enrollment of patients;
- manufacturing difficulties;
- failure of our clinical trials and clinical investigators to be in compliance with the FDA's GCP;
- failure of our third-party contract research organizations, clinical site organizations or other clinical trial managers, to satisfy their contractual duties, comply with regulations or meet expected deadlines;
- lack of efficacy during clinical trials; or
- unforeseen safety issues.

We do not know whether our clinical trials will need to be restructured or will be completed on schedule, if at all, or whether they will provide data necessary to support regulatory approval. Significant delays in clinical trials will impede our ability to commercialize our product candidates and generate revenue, and could significantly increase our development costs.

In addition, we utilize bovine-sourced materials to manufacture our product candidates. It is possible that future FDA regulations may require us to change the source of the bovine-sourced materials we use in our products or to cease using bovine-sourced materials. If we are required to use alternative materials in our products, and in the event that such alternative materials are available to us, or if we choose to change the materials used in our products in the

future, we would need to validate the new manufacturing process and run comparability trials with the reformulated product, which could delay our submission for regulatory approval of our product candidates and negatively impact the development and potential commercialization of our product candidates.

Table of Contents

If we fail to obtain the necessary regulatory approvals, or if such approvals are limited, we will not be able to commercialize our product candidates, and we will not generate product revenues.

Even if we comply with all FDA pre-approval regulatory requirements, the FDA may determine that our product candidates are not safe or effective, and we may never obtain regulatory approval for such product candidates. If we fail to obtain regulatory approval for some or all of our product candidates, we will have fewer commercial products, if any, and correspondingly lower product revenues, if any. Even if our product candidates receive regulatory approval, such approval may involve limitations on the indications and conditions of use or marketing claims for our products. Further, later discovery of previously unknown problems or AEs could result in additional regulatory restrictions, including withdrawal of products and addition of warnings or other statements on the product label.

With respect to LAVIV, which was approved in June 2011, as part of approval the FDA required us, based on clinical trial data, to conduct a 2,700 patient post-marketing study evaluating the risk of skin cancer in the injection site. This study is required to be completed by the end of 2016. We have been engaged in discussions with the FDA on the design of the post-marketing study, as we believe the original study design, especially the sample size, is no longer consistent with our current emphasis on azficel-T for vocal cord scarring and our decreased involvement with cosmetic applications. The FDA acknowledged that commercial volume since the marketing of LAVIV is inadequate to meet the original enrollment rate proposed but has required submission of actual enrollment data before considering a revision. We have initiated enrollment in the post-marketing study and have submitted the required biannual interim reports to the FDA containing this enrollment data, with the most recent being in January 2016. We continue to be actively engaged in discussions with the FDA about how to fulfill the original post-marketing study sample size requirement in light of the limited population of LAVIV users. Although we believe we will be able to reach an agreement with the FDA on this post-marketing study, to the extent we are unable to complete an acceptable post-marketing study, the FDA may determine to take action against us, including the withdrawal of its approval of LAVIV.

In jurisdictions outside the United States, we must receive marketing authorizations from the appropriate regulatory authorities before commercializing our product candidates. Regulatory approval processes outside the United States generally include requirements and risks similar to, and in many cases in excess of, the risks associated with FDA approval.

Our failure to comply with extensive governmental regulation may significantly affect our operating results.

Even if we obtain regulatory approval for some or all of our product candidates, we will continue to be subject to extensive ongoing requirements by the FDA, as well as by a number of foreign, national, state and local agencies. These regulations will impact many aspects of our operations, including testing, research and development, manufacturing, safety, efficacy, labeling, storage, quality control, AE reporting, import and export, record keeping, approval, distribution, advertising and promotion of our future products. We must also submit new or supplemental applications and obtain FDA approval for certain changes to an approved product, product labeling or manufacturing process. Application holders must also submit advertising and other promotional material to the FDA and report on ongoing clinical trials. The FDA enforces post-marketing regulatory requirements, including the cGMP requirements, through periodic unannounced inspections. We do not know whether we will pass any future FDA inspections. Failure to pass an inspection could disrupt, delay or shut down our manufacturing operations. Failure to comply with applicable regulatory requirements could result in, among other things:

- administrative or judicial enforcement actions;
- changes to advertising;
- failure to obtain regulatory approvals for our product candidates;
- revocation or suspension of regulatory approvals of products;
- product seizures or recalls;

- court-ordered injunctions;
- import detentions;
- delay, interruption or suspension of product manufacturing, distribution, marketing and sales; or
- civil or criminal sanctions.

The discovery of previously unknown problems with our products may result in restrictions on the products, including withdrawal from the market. In addition, the FDA may revisit and change its prior determinations with regard to the safety or efficacy of our future products. If the FDA's position changes, we may be required to change our labeling or cease to

Table of Contents

manufacture and market our future products. Even prior to any formal regulatory action, we could voluntarily decide to cease the distribution and sale or recall any of our future products if concerns about their safety or efficacy develop.

In their regulation of advertising and other promotion, the FDA and the FTC may issue correspondence alleging that some advertising or promotional practices are false, misleading or deceptive. The FDA and FTC are authorized to impose a wide array of sanctions on companies for such advertising and promotion practices, which could result in any of the following:

- incurring substantial expenses, including fines, penalties, legal fees and costs to comply with the FDA's requirements;
- changes in the methods of marketing and selling products;
- taking FDA mandated corrective action, which may include placing advertisements or sending letters to physicians rescinding previous advertisements or promotions; or
- disruption in the distribution of products and loss of sales until compliance with the FDA's position is obtained.

Improper promotional activities may also lead to investigations by federal or state prosecutors, and result in criminal and civil penalties. If we become subject to any of the above requirements, it could be damaging to our reputation and restrict our ability to sell or market our future products, and our business condition could be adversely affected. We may also incur significant expenses in defending ourselves.

Physicians may prescribe pharmaceutical or biologic products for uses that are not described in a product's labeling or differ from those tested by us and approved by the FDA. While such "off-label" uses are common and the FDA does not regulate physicians' choice of treatments, the FDA does restrict a manufacturer's communications on the subject of off-label use. Companies cannot promote FDA-approved pharmaceutical or biologic products for off-label uses, but under certain limited circumstances they may disseminate to practitioners' articles published in peer-reviewed journals. To the extent allowed by the FDA, we may disseminate peer-reviewed articles on our future products, if approved, to practitioners. If, however, our activities fail to comply with the FDA's regulations or guidelines, we may be subject to warnings from, or enforcement action by, the FDA or other regulatory or law enforcement authorities.

Our sales, marketing, and scientific/educational grant programs, if any in the future, must also comply with applicable requirements of the anti-fraud and abuse provisions of the Social Security Act, the False Claims Act, the federal anti-kickback law, and similar state laws, each as amended. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veteran's Health Care Act of 1992, each as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws. The distribution of product samples to physicians must comply with the requirements of the Prescription Drug Marketing Act.

Depending on the circumstances, failure to meet post-approval requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, or refusal to allow us to enter into supply contracts, including government contracts. Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity.

We are subject to significant regulation with respect to the manufacturing of our products.

Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with current Good Manufacturing Practices. These regulations govern manufacturing processes and procedures and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Our facilities and quality systems and the facilities and quality systems of some or all of our third party contractors and suppliers must pass inspection for compliance with

the applicable regulations as a condition of FDA approval of our products. In addition, the FDA may, at any time, audit or inspect a manufacturing facility, including our manufacturing facility, involved with the preparation of LAVIV, or our associated quality systems for compliance with the regulations applicable to the activities being conducted. The FDA also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulation occurs independent of such an inspection or audit, we or the FDA may require remedial measures that may be costly and/or time consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial

Table of Contents

sales, recalls, market withdrawals, seizures or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we fail to obtain or maintain orphan drug exclusivity for any of our product candidates, our competitors may sell products to treat the same conditions and our operations will be adversely impacted.

As part of our business strategy, we have obtained FDA orphan designation for FCX-007 and intend to seek orphan drug designation for FCX-013. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the U.S. The first company to obtain FDA approval for a designated orphan drug for a given rare disease receives marketing exclusivity for use of that drug for the stated condition for a period of seven years. Orphan drug exclusive marketing rights may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug or access to the biologic.

Because the extent and scope of patent protection for some of our product candidates is limited, orphan drug designation is especially important for our products that are eligible for orphan drug designation. For eligible product candidates, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug exclusivity for our product candidates that do not have broad patent protection, our competitors may then sell the same drug or biologic to treat the same condition which could adversely affect our operations.

Even though we have obtained orphan drug designation for FCX-007 and even if we obtain orphan drug designation for other product candidates, due to the uncertainties associated with developing biopharmaceutical products, we may not be the first to obtain regulatory approval for any particular orphan indication, which means that we may not obtain orphan drug exclusivity and could also potentially be blocked from approval until the first product’s orphan drug exclusivity period expires. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved and granted orphan drug exclusivity, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. Orphan drug designation does not shorten the regulatory review and approval process, nor does it provide any additional opportunities for review and guidance from the FDA during the review and approval process.

Even if we were to obtain approval for FCX-007 with the rare pediatric disease designation, the Rare Pediatric Disease Priority Review Voucher Program may no longer be in effect at the time of such approval.

FCX-007 has received rare pediatric disease designation from the FDA for the treatment of RDEB. The FDA defines a "rare pediatric disease" as a disease that affects fewer than 200,000 individuals in the U.S. primarily under the age of 18 years old. Under the FDA's Rare Pediatric Disease Priority Review Voucher program, upon the approval of a NDA or BLA for the treatment of a rare pediatric disease, the sponsor of such application would be eligible for a Rare Pediatric Disease Priority Review Voucher that can be used to obtain priority review for a subsequent NDA or BLA. The Priority Review Voucher may be sold or transferred an unlimited number of times. Congress has extended the Priority Review Voucher Program until September 30, 2016. This program has been subject to criticism, including by the FDA, and it is possible that even if we obtain approval for FCX-007 and qualify for such a Priority Review Voucher, the program may no longer be in effect at the time of approval.

We are largely dependent on the future commercial success of our product candidates.

Our ability to generate revenues and become profitable will depend in large part on the future commercial success of our product candidates. If any product that we commercialize in the future does not gain an adequate level of acceptance among physicians, patients and third parties, we may not generate significant product revenues or become profitable. Market acceptance of our products, and any other products that we commercialize, by physicians, patients and third party payors will depend on a number of factors, some of which are beyond our control, including:

- The efficacy, safety and other potential advantages in relation to alternative treatments;
- The relative convenience and ease of administration;
- The availability of adequate coverage or reimbursement by third parties, such as insurance companies and other healthcare payors, and by government healthcare programs, including Medicare and Medicaid;
- The prevalence and severity of adverse events;
- The cost of treatment in relation to alternative treatments, including generic products;

Table of Contents

- The extent and strength of our third party manufacturer and supplier support;
- The extent and strength of marketing and distribution support;
- The limitations or warnings contained in a product's FDA approved labeling; and
- Distribution and use restrictions imposed by the FDA or to which we agree as part of a mandatory risk evaluation and mitigation strategy or voluntary risk management plan

For example, even if our products have been approved by the FDA, physicians and patients may not immediately be receptive to them and may be slow to adopt them. In addition, even though we believe our product candidates have significant advantages to other treatment options, because no head-to-head trials comparing our product candidates to competing products will have been conducted, the prescribing information approved by the FDA would not contain claims that our product is safer or more effective than competitive products. Accordingly, promotion of our products will not reflect any comparative advantages that may exist. If our products do not achieve an adequate level of acceptance among physicians, patients and third party payors, we may not generate meaningful revenues from and we may not become profitable.

In order to commercialize any future product candidates, we will need to increase our manufacturing capacity and improve our manufacturing capabilities, which will require significant expenditures and regulatory approval.

We currently have limited manufacturing capacity. In order to commercialize any future product candidates, we will need to increase our manufacturing capacity. We are developing enhancements and alternatives to our current manufacturing process. If we have difficulties in increasing our manufacturing capacity and improving our capabilities, we will be limited in our ability to manufacture and commercialize our product candidates, if they are approved for marketing; and we may not be able to decrease our manufacturing costs. These difficulties could adversely affect our financial performance and damage our reputation. Even if we are successful in developing such enhancements or finding alternatives to our current process, such manufacturing changes will require additional expenditures, for which we may be required to seek external financing. In addition, our ability to increase our manufacturing capacity or modify our manufacturing processes will be subject to additional FDA review and approval.

Negative public opinion and increased regulatory scrutiny of gene therapies may damage public perception of our product candidates or adversely affect our ability to conduct our business or obtain regulatory approvals for our gene therapy product candidates.

Public perception may be influenced by claims that gene therapies are unsafe, and gene therapies may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians specializing in the treatment of those diseases that our product candidates target prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments they are already familiar with and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. Adverse events in our clinical trials, even if not ultimately attributable to our product candidates and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our potential product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

Future sales of our products are subject to adequate coverage, pricing and reimbursement from third-party payors, which are subject to increasing and intense pressure from political, social, competitive and other sources. Our inability to obtain and maintain adequate coverage, pricing or reimbursement, could have an adverse effect on our business.

Future sales of our product candidates, should they receive regulatory approval and be commercialized, are dependent, in large part, on the availability and extent of coverage, pricing and reimbursement from government health administration authorities, private health insurers and other organizations. When a new pharmaceutical product is approved, the availability of government and private reimbursement for that product may be uncertain, as is the pricing and amount for which that product will be reimbursed. The manner and level at which reimbursement is

provided for services related to our product candidates (e.g., for administration of our products to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our products.

Pricing and reimbursement for our products and services related to our products may be adversely affected by a number of factors, including:

Table of Contents

- changes in federal, state or foreign government regulations or private third-party payors' reimbursement policies;
- pressure by employers on private health insurance plans to reduce costs; and
- consolidation and increasing assertiveness of payors, including managed care organizations, health insurers, pharmacy benefit managers, government health administration authorities, private health insurers and other organizations, seeking price discounts or rebates in connection with the placement of our products on their formularies and, in some cases, the imposition of restrictions on access or coverage of particular drugs or pricing determined based on perceived value.

Our failure to maintain adequate coverage, pricing, or reimbursement for our products and services related to our products would have an adverse effect on our business, revenues and results of operation, could curtail or eliminate our ability to adequately fund research and development programs for the discovery and commercialization of new products, and could cause a decline in our stock price.

Drug pricing and other health care costs are under significant scrutiny in the U.S are subject to intense political and societal pressures which we anticipate will continue and escalate on a global basis. As a result, our business and reputation may be harmed, our stock price may be adversely impacted and experience periods of volatility, and our results of operations may be adversely impacted.

If the market opportunities for our product candidates are smaller than we believe they are, our results of operations may be adversely affected and our business may suffer.

We focus our research and product development on treatments of diseases affecting the skin, connective tissue and joints. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates may prove to be incorrect and new studies or clinical trials may change the estimated incidence or prevalence of these diseases. The number of patients in the U.S. and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

If any of our approved products were to become the subject of problems related to their efficacy, safety, or otherwise, our business would be seriously harmed.

LAVIV, in addition to any other of our product candidates that may be approved by the FDA, will be subject to continual review by the FDA, and we cannot assure you that newly discovered or developed safety issues will not arise. For all of our product candidates, the FDA has required us to pay special attention to potential skin cancer and hypersensitivity reactions at the site of injection and, while we have seen no issues to date, we cannot rule out that issues may arise in the future. With the use of any newly marketed drug by a wider patient population, serious adverse events ("AE's") may occur from time to time that initially do not appear to relate to the drug itself. Any safety issues could cause us to suspend or cease marketing of our approved products, cause us to modify how we market our approved products, subject us to substantial liabilities, and adversely affect our financial condition and business.

If physicians do not follow our established protocols, the efficacy and safety of our product candidates may be adversely affected.

We are dependent on physicians and other healthcare professionals to follow our established protocols both as to the administration and the handling of our product candidates in connection with our clinical trials, and we continue to be dependent on physicians and other healthcare professionals to follow such protocols after our product candidates are commercialized. The treatment protocol requires each physician to verify the patient’s name and date of birth with the patient and the patient records immediately prior to injection. In the event more than one patient’s cells are delivered to a physician or we deliver the wrong patient’s cells to the physician, which has occurred in the past, it is the physician’s obligation to follow the treatment protocol and assure that the patient is treated with the correct cells. If the physicians and other healthcare professionals do not follow our protocol, the efficacy and safety of our product candidates may be adversely affected.

30

Table of Contents

Our competitors in the pharmaceutical, medical device and biotechnology industries may have superior products, manufacturing capabilities, financial resources or marketing position.

The human healthcare products and services industry is extremely competitive. Our competitors include major pharmaceutical, medical device and biotechnology companies. Most of these competitors have more extensive research and development and marketing and manufacturing capabilities than we do, as well as greater financial resources. Our future success will depend on our ability to develop and market effectively our products against those of our competitors. If our products cannot compete effectively in the marketplace, our results of operations and financial position will suffer.

Our cell and gene therapy product candidates may face competition in the future from biosimilars.

With the enactment of the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), as part of the Patient Protection and Affordable Care Act, an abbreviated pathway for the approval of follow-on biological products was created. The new abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as “interchangeable” with an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. This data exclusivity does not prevent another company from developing a product that is highly similar to the original branded product, generating its own data and seeking approval. Data exclusivity only assures that another company cannot rely upon the data within the innovator’s application to support the biosimilar product’s approval.

In his proposed budget for fiscal year 2014, President Obama proposed to cut this 12-year period of exclusivity down to seven years. He also proposed to prohibit additional periods of exclusivity due to minor changes in product formulations, a practice often referred to as “evergreening.” It is possible that Congress may take these or other measures to reduce or eliminate periods of exclusivity.

Although final implementation of the BPCIA is not yet complete, such FDA implementation could have a material adverse effect on the future commercial prospects for our product candidates.

We may be liable for product liability claims not covered by insurance.

Physicians, patients and clinical trial participants who have used our products in the past or who use them in the future may bring product liability claims against us. While we have taken, and continue to take, what we believe are appropriate precautions, we may be unable to avoid significant liability exposure. We currently keep in force product liability insurance, although such insurance may not be adequate to fully cover any potential claims or may lapse in accordance with its terms prior to the assertion of claims. We may be unable to obtain product liability insurance in the future, or we may be unable to do so on acceptable terms. Any insurance we obtain or have obtained in the past may not provide adequate coverage against any asserted claims. In addition, regardless of merit or eventual outcome, product liability claims may result in:

•diversion of management’s time and attention;
•expenditure of large amounts of cash on legal fees, expenses and payment of damages;
•decreased demand for our products or any of our future products and services; or
•injury to our reputation.

If we are the subject of any future product liability claims, our business could be adversely affected, and if these claims are in excess of insurance coverage, if any, that we may possess, our financial position will suffer.

Risks Related to Our Dependence on Third Parties

We will incur additional expenses in connection with our exclusive channel collaboration agreements with Intrexon.

Pursuant to our exclusive channel collaboration agreements with Intrexon, we are responsible for future research, development and commercialization expenses of product candidates developed under such collaborations, including FCX-007, FCX-013 and our gene therapy program for arthritis, the effect of which we expect will increase the level of our overall research and development expenses going forward. Although all manufacturing, pre-clinical studies and human clinical trials are expensive and difficult to design and implement, costs associated with the manufacturing, research and development of gene therapy product candidates are generally greater in comparison to small molecule product candidates. We have added personnel and expect to add additional personnel, either directly or through consulting arrangements, to support our exclusive channel collaborations with Intrexon.

31

Table of Contents

Because development activities are determined pursuant to a joint steering committee comprised of Intrexon and ourselves and we have limited experience, future development costs associated with this program may be difficult to anticipate and exceed our expectations. Our actual cash requirements may vary materially from our current expectations for a number of other factors that may include, but are not limited to, unanticipated technical challenges, changes in the focus and direction of our development activities or adjustments necessitated by changes in the competitive landscape in which we operate. If we are unable to continue to financially support such collaboration due to our own working capital constraints, we may be forced to discontinue the collaboration or delay our activities.

We may not be able to retain the exclusive rights licensed to us by Intrexon to develop and commercialize our gene therapy product candidates.

Pursuant to our exclusive channel collaboration agreements, we are using Intrexon's technology in connection with various product candidates. The collaboration agreements grant us a license to use patents and other intellectual property of Intrexon in connection with the research, development, and commercialization of collaboration products within "Fields" that we set forth above in the "Item 1. Business - Intrexon Collaboration".

The exclusive channel collaboration agreements may be terminated by Intrexon if we fail to exercise diligent efforts in developing products through the collaboration or if we elect not to pursue the development of a therapy in a "Field" identified by Intrexon that is a "Superior Therapy" as defined in the agreement. Upon such termination, the products covered by the applicable exclusive channel collaboration agreement in active and ongoing Phase II or III clinical trials or later stage development through the exclusive channel collaboration agreement shall be entitled to be continued by us with a continuation of the related royalties for such products, and all rights to products covered by the exclusive channel collaboration agreement still in an earlier stage of development shall revert to Intrexon.

There can be no assurance that we will be able to successfully perform under the exclusive channel collaboration agreements and if either agreement is terminated it may prevent us from achieving our business objectives and our business may be harmed.

We depend on third parties to conduct our pre-clinical studies and clinical trials, which may result in costs and delays that prevent us from obtaining regulatory approval or successfully commercializing our product candidates.

We engage third parties to perform various aspects of our pre-clinical studies and clinical trials. For instance, we obtain genetically-modified material from a sole source supplier in connection with the pre-clinical development of RDEB. We depend on these third parties to perform these activities on a timely basis in accordance with the protocol, good laboratory practices, good clinical practices, and other regulatory requirements. Our reliance on these third parties for pre-clinical and clinical development activities reduces our control over these activities. Accordingly, if these parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, our pre-clinical studies and clinical trials may be extended, delayed, terminated or our data may be rejected by the FDA. For example, our sole source supplier of genetically-modified material in connection with the pre-clinical development of RDEB were to cease to be able to supply genetically-modified material to us, or decline to supply genetically-modified material to us, our RDEB program would be delayed until we obtained an alternative source, which could take a considerable length of time. If it became necessary to replace a third party that was assisting with one of our pre-clinical studies or clinical trials, we believe that there are a number of other third-party contractors that could be engaged to continue these activities, although it may result in a delay of the applicable pre-clinical study or clinical trial. If there are delays in testing or obtaining regulatory approvals as a result of a third party's failure to perform, our drug discovery and development costs will likely increase, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates.

We have limited manufacturing capacity and any manufacturing difficulties, disruptions or delays could limit supply of our products and or adversely affect our ability to conduct our clinical trials.

Manufacturing biologic products is difficult, complex and highly regulated. We currently manufacture LAVIV and our non-genetically modified cell therapy product candidates at our facility in Exton, PA. We outsource the manufacturing of our genetically modified product candidates to a contract manufacturer in Mountain View, CA. Our ability to adequately and timely manufacture and supply our products is dependent on the operation of our sole facility

and those of our contract manufacturer, which may be impacted by, among other things:

- availability, performance, or contamination of raw materials and components used in the manufacturing process, particularly those for which we have no other source or supplier;
- quality of incoming biopsy samples;

Table of Contents

- capacity of our facility and those of contract manufacturer;
- the performance of information technology systems;
- compliance with regulatory requirements;
- inclement weather and natural disasters;
- changes in forecasts of future demand for product components;
- timing and actual number of production runs for product components;
- potential facility contamination by microorganisms or viruses;
- updating of manufacturing specifications; and
- product quality success rates and yields.

If the efficient manufacture and supply of our products is interrupted, we may experience delayed shipments or supply constraints. If we are at any time unable to provide an uninterrupted supply of our products to patients, we may lose patients and physicians may elect to prescribe competing therapeutics instead of our products, which could materially and adversely affect our product sales and results of operations. In addition, if we are unable to supply our clinical trials due to manufacturing limitations, our trials may be delayed or compromised.

Our manufacturing processes and those of our contract manufacturer must undergo a potentially lengthy FDA approval process, as well as other regulatory approval processes, and are subject to continued review by the FDA and other regulatory authorities. It is a multi-year process to build and license a new manufacturing facility and it can take significant time to qualify and license a contract manufacturer.

If regulatory authorities determine that we or our contract manufacturer or certain of our third-party service providers have violated regulations or if they restrict, suspend or revoke our prior approvals, they could prohibit us from manufacturing our products or conducting clinical trials or selling our marketed products until we or the affected third-party service providers comply, or indefinitely. Because our third-party service providers are subject to FDA and, potentially, in the future, foreign regulatory authorities, alternative qualified third-party service providers may not be available on a timely basis or at all. If we or our third-party service providers cease or interrupt production or if our third-party service providers fail to supply materials, products or services to us, we may experience delayed shipments, and supply constraints for our products.

Our research, development and manufacturing operations depend on one facility each for both our cell therapy and gene therapy product candidates. If such facility is destroyed or is out of operation for a substantial period of time, our business will be adversely impacted.

We currently conduct our research, development and manufacturing operations related to LAVIV and our non-genetically modified product candidates in one facility located in Exton, Pennsylvania. We currently outsource our research, development and manufacturing operations related to our gene therapy product candidates to a contract manufacturer that uses one facility located in Mountain View, California.

If regulatory, manufacturing or other problems require us to discontinue production at either facility, we will not be able to supply our product to our customers or have supplies for our clinical trials, which would adversely impact our business. If either facility or the equipment in it is significantly damaged or destroyed by fire, flood, power loss or similar events, we may not be able to quickly or inexpensively replace our manufacturing capacity or replace our facility at all. In the event of a temporary or protracted loss of either facility or equipment, we might not be able to transfer manufacturing to a third party. Even if we could transfer manufacturing to a third party, the shift would likely be expensive and time-consuming, particularly since the new facility would need to comply with the necessary regulatory requirements and we would need FDA approval before any products manufactured at that facility could be sold or used.

Risks Related to Our Intellectual Property

If we or our licensors are unable to protect our intellectual property rights or if our intellectual property rights are inadequate for our technologies, products and product candidates, our competitive position could be harmed.

Our commercial success will depend in large part on our, and our licensors, ability to obtain and maintain patent and other intellectual property protection in the U.S. and other countries with respect to our proprietary technology and products. We rely on trade secret, patent, copyright and trademark laws, and confidentiality, licensing and other agreements with

Table of Contents

employees and third parties, all of which offer only limited protection. We seek to protect our proprietary position by filing and prosecuting patent applications in the U.S. and abroad related to our novel technologies and products that are important to our business.

The patent positions of biopharmaceutical companies generally are highly uncertain, involve complex legal and factual questions and have in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patents, including those patent rights licensed to us by third parties, are highly uncertain. The steps we or our licensors have taken to protect our proprietary rights may not be adequate to preclude misappropriation of our proprietary information or infringement of our intellectual property rights, both inside and outside the U.S. Further, the examination process may require us or our licensors to narrow the claims for our pending patent applications, which may limit the scope of patent protection that may be obtained if these applications issue. The rights already granted under any of our currently issued patents or those licensed to us and those that may be granted under future issued patents may not provide us with the proprietary protection or competitive advantages we are seeking. If we or our licensors are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection obtained is not sufficient, our competitors could develop and commercialize technology and products similar or superior to ours, and our ability to successfully commercialize our technology and products may be adversely affected. It is also possible that we or our licensors will fail to identify patentable aspects of inventions made in the course of our development and commercialization activities before it is too late to obtain patent protection on them.

With respect to patent rights, we do not know whether any of the pending patent applications for any of our therapies will result in the issuance of patents that protect our technology or products, or if any of our or our licensors' issued patents will effectively prevent others from commercializing competitive technologies and products. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing or in some cases not at all, until they are issued as a patent. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

Our issued patents, those that may be issued in the future or those licensed or acquired by us, may be challenged, invalidated or circumvented, and the rights granted under any issued patent may not provide us with proprietary protection or competitive advantages against competitors with similar technology. In particular, we do not know if competitors will be able to design variations on our treatment methods to circumvent our current and anticipated patent claims. Furthermore, competitors may independently develop similar technologies or duplicate any technology developed by us.

Our pending applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, issued patents that we own or have licensed from third parties may be challenged in the courts or patent offices in the U.S. and abroad. Such challenges may result in the loss of patent protection, the narrowing of claims in such patents or the invalidity or unenforceability of such patents, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection for our technology and products. Protecting against the unauthorized use of our or our licensor's patented technology, trademarks and other intellectual property rights is expensive, difficult and may in some cases not be possible. In some cases, it may be difficult or impossible to detect third-party infringement or misappropriation of our intellectual property rights, even in relation to issued patent claims, and proving any such infringement may be even more difficult.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could harm our business.

Our commercial success depends upon our ability to develop, manufacture, and if approved, market and sell our product candidates and to use our related proprietary technologies. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products or product candidates, including interference, post grant review, inter partes review or derivation proceedings before the U.S. Patent and Trademark Office, or USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue commercializing our products. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Under certain circumstances, we could be forced, including by court order, to cease commercializing our products and then expend time and funding to redesign our product and/or product candidates so that it does not infringe others' patents while still allowing us to compete in the market with a substantially similar product. In addition, in any such proceeding or litigation, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our products or force us to cease some of our business operations, which could materially

Table of Contents

harm our business. Any claims by third parties that we have misappropriated their confidential information or trade secrets could have a similar negative impact on our business. In addition, our involvement in any of these proceedings may cause us to incur substantial costs and result in diversion of management and technical personnel. Furthermore, parties making claims against us may be able to obtain injunctive or other equitable relief that could effectively block our ability to develop, commercialize and sell products, and could result in the award of substantial damages against us.

We believe that use of our product candidates in clinical trials falls within the scope of the exemptions provided by 35 U.S.C. Section 271(e) in the U.S., which exempts from patent infringement liability activities reasonably related to the development and submission of information to the FDA. As our product candidates progresses toward regulatory approval and commercialization, the possibility of a patent infringement claim against us increases. We attempt to ensure that our product candidates and the methods we employ to manufacture them, as well as the methods for their use we intend to promote, do not infringe other parties' patents and other proprietary rights. There can be no assurance they do not, however, and competitors or other parties may assert that we infringe their proprietary rights in any event.
We may not be able to protect our intellectual property rights throughout the world.
Filing, prosecuting and defending patents on all of our product candidates throughout the world would be prohibitively expensive, and our or our licensors' intellectual property rights in some countries outside the U.S. can be less extensive than those in the U.S. In addition, the laws and practices of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we and our licensors may not be able to prevent third parties from practicing our and our licensors' inventions in all countries outside the U.S., or from selling or importing products made using our and our licensors' inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products, and may export otherwise infringing products to territories where we or our licensors have patent protection, but where enforcement is not as strong as that in the U.S. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our or our licensor's patents or marketing of competing products in violation of our proprietary rights generally in those countries. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business, could put our and our licensors' patents at risk of being invalidated or interpreted narrowly and our and our licensors' patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensors. We or our licensors may not prevail in any lawsuits that we or our licensors initiate and the damages or other remedies awarded, if any, may not be commercially meaningful.

The laws of certain foreign countries may not protect our rights to the same extent as the laws of the U.S., and these foreign laws may also be subject to change. For example, methods of treatment and manufacturing processes may not be patentable in certain jurisdictions, and the requirements for patentability may differ in certain countries, particularly developing countries. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for, and launch generic versions of our products. Many countries, including European Union countries, India, Japan and China, have compulsory licensing laws under which a patent owner may be compelled under certain circumstances to grant licenses to third parties. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our and our licensors' efforts to

enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time.

Given the amount of time required for the development, testing and regulatory review of products, such as LAVIV, and our other products candidates patents protecting such candidates might expire before or shortly after such candidates are commercialized. We expect to seek extensions of patent terms in the U.S. and, if available, in other countries where we are prosecuting patents. In the U.S., the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). However, the applicable authorities, including the FDA and the USPTO in the U.S., and any equivalent regulatory authority in other countries, may not agree with our assessment of whether

Table of Contents

such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and pre-clinical data and launch their product earlier than might otherwise be the case.

Changes in patent law, including recent patent reform legislation, could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve technological and legal complexity, and obtaining and enforcing pharmaceutical patents is costly, time-consuming, and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection. For example, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our and our licensors' ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our and our licensors' ability to obtain new patents or to enforce existing patents and patents we and our licensors may obtain in the future. Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our and our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents.

In September 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the U.S. transitioned in March 2013 to a "first to file" system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO and may become involved in opposition, derivation, reexamination, post grant review, inter-partes review or interference proceedings challenging our patent rights or the patent rights of our licensors. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our or our licensors' patent rights, which could adversely affect our competitive position. The Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents and those licensed to us.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submissions, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our product candidates, our competitive position would be adversely affected.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

To protect our proprietary know-how and our inventions for which patents may be unobtainable or difficult to obtain, and to maintain our competitive position, we rely on trade secret protection and confidentiality agreements. To this end, it is our general policy to require our employees, consultants, advisors, and contractors to enter into agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries, and inventions important to our business. These agreements may not provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information. Moreover, we may not be able to obtain adequate remedies for any breaches of these agreements. Our trade secrets may also be obtained by third parties by other means, such as breaches of our physical or computer security systems. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States

Table of Contents

are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets, know-how or other proprietary information is disclosed, the value of our trade secrets, know-how and other proprietary rights would be significantly impaired and our business and competitive position would suffer.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful and have a material adverse effect on the success of our business.

Competitors may infringe our patents or misappropriate or otherwise violate our intellectual property rights. To counter infringement or unauthorized use, litigation may be necessary in the future to enforce or defend our intellectual property rights, to protect our trade secrets or to determine the validity and scope of our own intellectual property rights or the proprietary rights of others. Also, third parties may initiate legal proceedings against us or our licensors to challenge the validity or scope of intellectual property rights we own or control. These proceedings can be expensive and time consuming. Many of our current and potential competitors have the ability to dedicate substantially greater resources to defend their intellectual property rights than we can. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating our intellectual property. Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results. In addition, in an infringement proceeding, a court may decide that a patent owned by or licensed to us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of shares of our common stock.

We may be subject to claims by third parties asserting that our licensors, employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees and our licensors' employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive

advantage. The following examples are illustrative:

- others may be able to make compounds that are the same as or similar to our product candidates, but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or any strategic partners might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed;
- we or our licensors might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;

Table of Contents

- issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges;
- our competitors might conduct research and development activities in the U.S. and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Risks Related to Business Operations

We are dependent on our executives and other key professionals and the loss of any of these individuals could harm our business.

We are dependent on the efforts of our executives and other key scientific, manufacturing and quality personnel. The loss of any of these individuals, or our inability to recruit and train additional key personnel in a timely manner, could materially and adversely affect our business and our future prospects. A loss of one or more of our current executives or other key professionals could severely and negatively impact our operations. All of our employees, including our chief executive officer, are employed “at-will,” and any of them may elect to pursue other opportunities at any time. We have no present intention of obtaining key man life insurance on any of our executive officers or key professionals.

We may need to attract, train and retain additional experienced executives and other key professionals in the future.

In the future, we may need to seek additional executives and other key professionals. There is a high demand for experienced executive, scientific, manufacturing and quality personnel in our industry. We do not know whether we will be able to attract, train and retain such experienced personnel in the future, which could have a material adverse effect on our business, financial condition and results of operations.

Our results of operations may be adversely affected by current and potential future healthcare reforms.

In the U.S., federal and state legislatures, health agencies and third-party payors continue to focus on containing the cost of health care. Legislative and regulatory proposals and enactments to reform health care insurance programs could significantly influence the manner in which our products are prescribed and purchased. For example, provisions of the Patient Protection and Affordable Care Act ("PPACA") have resulted in changes in the way health care is paid for by both governmental and private insurers, including increased rebates owed by manufacturers under the Medicaid Drug Rebate Program, annual fees and taxes on manufacturers of certain branded prescription drugs, the requirement that manufacturers participate in a discount program for certain outpatient drugs under Medicare Part D and the expansion of the number of hospitals eligible for discounts under Section 340B of the Public Health Service Act. These changes have had and are expected to continue to have a significant impact on our business.

There is also significant economic pressure on state budgets that may result in states increasingly seeking to achieve budget savings through mechanisms that limit coverage or payment for our drugs. In recent years, some states have considered legislation and ballot initiatives that would control the prices of drugs, including laws to allow importation of pharmaceutical products from lower cost jurisdictions outside the U.S. and laws intended to impose price controls on state drug purchases. State Medicaid programs are increasingly requesting manufacturers to pay supplemental rebates and requiring prior authorization by the state program for use of any drug for which supplemental rebates are not being paid. Government efforts to reduce Medicaid expenses may lead to increased use of managed care organizations by Medicaid programs. This may result in managed care organizations influencing prescription decisions for a larger segment of the population and a corresponding constraint on prices and reimbursement for our products. In addition, under the PPACA, as states implement their health care marketplaces or operate under the

federal exchange, the impact on drug manufacturers will depend in part on the formulary and benefit design decisions made by insurance sponsors or plans participating in these programs. It is possible that we may need to provide discounts or rebates to such plans in order to maintain favorable formulary access for our future products, which could have an adverse impact on our sales and results of operations.

If we fail to comply with federal and state healthcare laws, including fraud and abuse and health information privacy and security laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected.

Table of Contents

As a biopharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. For example, we could be subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include, among others:

- The federal Anti-Kickback Statute, which constrains our business activities, including our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, either the referral of an individual or the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- Federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;
- Requirements to report annually to CMS certain financial arrangements with physicians and teaching hospitals, as defined in the ACA and its implementing regulations, including reporting any "transfer of value" made or distributed to teaching hospitals, prescribers, and other healthcare providers and reporting any ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations during the preceding calendar year; and
- State and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts certain payments that may be made to healthcare providers and entities; state laws that require drug manufacturers to report information related to payments and other transfer of value to physicians and other healthcare providers and entities; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has further strengthened these laws. For example, the ACA, among other things, amends the intent requirement of the federal anti-kickback and certain criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Moreover, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

To the extent that any of our product candidates is ultimately sold in a foreign country, we may be subject to similar foreign laws and regulations.

If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including administrative, civil and criminal penalties, damages, fines, exclusion from participation in United States federal or state health care programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations any of which could materially adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of

investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

Table of Contents

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing manufacturing and laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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

Despite the implementation of security measures, our internal computer systems, and those of our contract research organizations, contract manufacturing organization, and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. System failures, accidents or security breaches could cause interruptions in our operations or the unauthorized transfer of our proprietary information, and could result in a material disruption of our clinical activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs. For example, the loss of clinical trial data from completed or ongoing clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach was to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

Our ability to use net operating loss carryforwards to reduce future tax payments may be limited or restricted.

We have generated significant net operating loss carryforwards ("NOL's") as a result of our incurrence of losses and our conduct of research activities since inception. We generally are able to carry NOL's forward to reduce our tax liability in future years. However, our ability to utilize the NOL's is subject to the rules of Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "Code"). Those sections generally restrict the use of NOL's after an "ownership change." An ownership change occurs if, among other things, the stockholders (or specified groups of stockholders) who own or have owned, directly or indirectly, 5% or more of a corporation's common stock or are otherwise treated as 5% stockholders under Section 382 of the Code and the United States Treasury Department regulations promulgated thereunder increase their aggregate percentage ownership of that corporation's stock by more than 50 percentage points over the lowest percentage of the stock owned by these stockholders over the applicable testing period. In the event of an ownership change, Section 382 imposes an annual limitation on the amount of taxable income a corporation may offset with NOL carry forwards and Section 383 imposes an annual limitation on the amount of tax a corporation may offset with carry forwards. Any unused annual limitation may be carried over to later years until the applicable expiration date for the respective NOL carry forwards. We have completed several

financings since our inception which we believe have resulted in “ownership changes” within the meaning of Section 382. We may also experience ownership changes in the future as a result of additional financings and subsequent shifts in our stock ownership. As a result, our NOL's may be subject to limitations and we may be required to pay taxes earlier and in larger amounts than would be the case if our NOL's were freely usable.

Table of Contents

Risks Related to Ownership of our Common Stock

The trading price of the shares of our common stock has been highly volatile, and purchasers of our common stock could incur substantial losses.

Our stock began trading on NYSE MKT on May 17, 2013 and then on the NASDAQ Stock Market LLC ("NASDAQ") on August 29, 2014. Between May 17, 2013 and December 31, 2015, our common stock has traded between $2.28 and $7.60. Our stock price could be subject to wide fluctuations in response to a variety of factors, which include:

- whether our clinical trials can be conducted within the timeframe that we expect and whether such trials will yield positive results;
- whether our collaborations with Intrexon can be advanced with positive results within the timeframe and budget that we expect;
- changes in laws or regulations applicable to our products or product candidates, including but not limited to clinical trial requirements for approvals;
- unanticipated serious safety concerns related to the use of our products or product candidates;
- a decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- our ability to increase our manufacturing capacity and reduce our manufacturing costs through the improvement of our manufacturing process, our ability to validate any such improvements with the relevant regulatory agencies and our ability to accomplish the foregoing on a timely basis;
- adverse regulatory decisions;
- the introduction of new products or technologies offered by us or our competitors;
- negative public opinion or perception of cell and gene therapies;
- the inability to effectively manage our growth;
- actual or anticipated variations in quarterly operating results;
- the failure to meet or exceed the estimates and projections of the investment community;
- the perception of the biopharmaceutical industry by the public, legislatures, regulators and the investment community;
- the overall performance of the U.S. equity capital markets and general political and economic conditions;
- announcements of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key personnel;
- the trading volume of our common stock; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and the stock of biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Randal J. Kirk and certain of his affiliates (including Intrexon) own a substantial percentage of our common stock and will be able to exert significant influence over matters subject to stockholder approval.

As of March 4, 2016, Randal J. Kirk and certain of his affiliates (including Intrexon, our collaboration partner on our gene therapy programs) beneficially owned approximately 16.6 million shares, or approximately 38%, of our common stock. Mr. Kirk and his affiliates may have interests that conflict with our other stockholders and, if acting together, have the ability to significantly influence the outcome of matters submitted to our stockholders for approval, including the election and removal of directors and any merger, consolidation or sale of all or substantially all of our assets. This

concentration of ownership could delay or prevent any acquisition of our company on terms that other stockholders may desire.

Table of Contents

Additionally, two of our directors, Julian Kirk (who is the son of Randal J. Kirk) and Marcus Smith, are employees of Third Security, LLC, which is an affiliate of Randal J. Kirk.

Our operating results may fluctuate significantly in the future, which may cause our results to fall below the expectations of securities analysts, stockholders and investors.

Our operating results may fluctuate significantly in the future as a result of a variety of factors, many of which are outside of our control. These factors include, but are not limited to:

- the timing, implementation and cost of our pre-clinical studies and clinical trials;
- expenses in connection with our exclusive channel collaboration agreements with Intrexon;
- the timely and successful implementation of improved manufacturing processes;
- our ability to attract and retain personnel with the necessary strategic, technical and creative skills required for effective operations;
- the amount and timing of expenditures by practitioners and their patients;
- introduction of new technologies;
- product liability litigation, class action and derivative action litigation, or other litigation;
- the amount and timing of capital expenditures and other costs relating to the expansion of our operations;
- the state of the debt and/or equity capital markets at the time of any proposed offering we choose to initiate;
- our ability to successfully integrate new acquisitions into our operations;
- government regulation and legal developments regarding our product candidates in the United States and in the foreign countries in which we may operate in the future; and
- general economic conditions.

As a strategic response to changes in the competitive environment, we may from time to time make pricing, service, technology or marketing decisions or business or technology acquisitions that could have a material adverse effect on our operating results. Due to any of these factors, our operating results may fall below the expectations of securities analysts, stockholders and investors in any future period, which may cause our stock price to decline.

Future sales of our common stock may depress our stock price.

The market price of our common stock could decline as a result of sales of substantial amounts of our common stock in the public market, or as a result of the perception that these sales could occur, which could occur if we issue a large number of shares of common stock (or securities convertible into our common stock) in connection with a future financing, as our common stock is trading at low levels. These factors could make it more difficult for us to raise funds through future offerings of common stock or other equity securities. As of the date of this report, all of our outstanding shares held by non-affiliates are freely transferable without restriction or further registration under the Securities Act. In addition to our common stock outstanding, as of December 31, 2015, we had warrants and options outstanding that were exercisable for a total of 7,146,718 shares of common stock.

We have not declared any dividends on our common stock to date, and we have no intention of declaring dividends in the foreseeable future.

The decision to pay cash dividends on our common stock rests with our Board of Directors and will depend on our earnings, unencumbered cash, capital requirements and financial condition. We do not anticipate declaring any dividends in the foreseeable future, as we intend to use any excess cash to fund our operations. Investors in our common stock should not expect to receive dividend income on their investment, and investors will be dependent on the appreciation of our common stock to earn a return on their investment.

Table of Contents

Provisions in our charter documents could prevent or delay stockholders' attempts to replace or remove current members of our Board of Directors.

Our charter documents provide for staggered terms for the members of our Board of Directors. Our Board of Directors is divided into three staggered classes, and each director serves a term of three years. At stockholders' meetings, only those directors comprising one of the three classes will have completed their term and be subject to re-election or replacement.

In addition, our Board of Directors is authorized to issue "blank check" preferred stock, with designations, rights and preferences as they may determine. Accordingly, our Board of Directors has in the past and may in the future, without stockholder approval, issue shares of preferred stock with dividend, liquidation, conversion, voting or other rights that could adversely affect the voting power or other rights of the holders of our common stock. This type of preferred stock could also be issued to discourage, delay or prevent a change in our control.

The use of a staggered Board of Directors and the ability to issue "blank check" preferred stock are traditional anti-takeover measures. These provisions in our charter documents make it difficult for a majority stockholder to gain control of the Board of Directors and of our company. These provisions may be beneficial to our management and our Board of Directors in a hostile tender offer and may have an adverse impact on stockholders who may want to participate in such a tender offer, or who may want to replace some or all of the members of our Board of Directors.

Provisions in our bylaws provide for indemnification of officers and directors, which could require us to direct funds away from our business and future products.

Our bylaws provide for the indemnification of our officers and directors. We have in the past and may in the future be required to advance costs incurred by an officer or director and to pay judgments, fines and expenses incurred by an officer or director, including reasonable attorneys' fees, as a result of actions or proceedings in which our officers and directors are involved by reason of being or having been an officer or director of our company. Funds paid in satisfaction of judgments, fines and expenses may be funds we need for the operation of our business and the development of our product candidates, thereby affecting our ability to attain profitability.

Provisions of the warrants issued in connection with certain of our prior financings provide for preferential treatment to the holders of the warrants and could impede a sale of the Company.

The warrants we issued in connection with certain of our prior financings gives each holder the option to receive a cash payment based on a Black-Scholes valuation upon our change of control or upon our failure to be listed on any trading market. We are required, at the warrant holder's option, exercisable at any time concurrently with, or within 30 days after, the announcement of a fundamental transaction, to redeem all or any portion of these warrants from the warrant holder by paying to the holder an amount of cash equal to the Black-Scholes value of the remaining unexercised portion of the warrant on or prior to the date of the consummation of such fundamental transaction.

An active market for our common stock may not be sustained.

In the past, we have had a limited, volatile and sporadic public trading market for our common stock. Although our common stock is listed on NASDAQ, an active trading market for our common stock may not be sustained, especially given the large percentage of our common stock held by our affiliates. If an active market for our common stock is not sustained, it may be difficult for our stockholders to sell shares without depressing the market price for our common stock.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. If one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Item 1B. Unresolved Staff Comments

None.

Table of Contents

Item 2. Properties

Our corporate office and manufacturing facility are located at 405 Eagleview Boulevard, Exton, Pennsylvania. This location consists of approximately 17,500 square feet of manufacturing and laboratory space and 69,000 square feet of office space, which we lease pursuant to a lease agreement that expires on March 31, 2023. We believe this facility is suitable for our current needs.

Item 3. Legal Proceedings

We are not a party to any pending legal proceedings.

Item 4. Mine Safety Disclosure

Not applicable.

Part II

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

Market Information

Our common stock trades under the symbol "FCSC." Our stock traded on the Over the Counter Bulletin Board ("OTCBB") from October 21, 2009 until May 16, 2013. On May 17, 2013 our stock began trading on the NYSE MKT. On August 28, 2014, the Company delisted its common stock from the NYSE MKT and began trading on NASDAQ. The following table sets forth, for the indicated periods in which we traded on the NYSE MKT and NASDAQ, the high and low intra-day sales prices per share for our common stock.

	High	Low
Year Ended December 31, 2015		
First Quarter	$5.99	$2.38
Second Quarter	$6.40	$3.25
Third Quarter	$7.60	$3.68
Fourth Quarter	$6.18	$3.50
Year Ended December 31, 2014		
First Quarter	$6.30	$4.00
Second Quarter	$5.23	$2.70
Third Quarter prior to August 29, 2014 (NYSE MKT until the date we began trading on the NASDAQ)	$4.31	$2.88
Third Quarter (from August 29, 2014 to September 30, 2014)	$3.40	$2.60
Fourth Quarter	$3.25	$2.28

The closing price of our common stock on March 4, 2016 was $2.70 as reported on NASDAQ.

Holders of Record

As of March 4, 2016, there were 43,898,785 shares of our common stock outstanding. There were approximately 145 stockholders of record at March 4, 2016. Because many of our shares are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

Dividends

We have never declared or paid any cash dividend on our common stock and our Board of Directors does not intend to do so in the foreseeable future. The declaration and payment of dividends in the future, of which there can be no assurance, will be determined by the Board of Directors in light of conditions then existing, including earnings, financial condition, capital requirements and other factors.

44

Table of Contents

Securities Authorized for Issuance under Equity Compensation Plans

Information regarding securities authorized for issuance under equity compensation plans is incorporated by reference into the information in Part III, Item 12 of this Annual Report on Form 10-K.

Recent Sales of Unregistered Securities

All information regarding the issuance of our securities during the quarter ended December 31, 2015 have been previously disclosed in current reports we have filed on Form 8-K or in quarterly reports we have filed on Form 10-Q. We did not issue any unregistered equity securities during the quarter ended December 31, 2015.

Stock Performance Graph

The following graph compares the cumulative total return on our common stock relative to the cumulative total returns of the NASDAQ composite index and the NASDAQ Biotechnology index for the period from December 31, 2010 through December 31, 2015. An investment of $100 (with reinvestment of all dividends) is assumed to have been made in our common stock and in each of the indexes on December 31, 2010 and its relative performance is tracked through December 31, 2015.

	As of 12/31/2010	12/31/2011	12/31/2012	12/31/2013	12/31/2014	12/31/2015
Fibrocell Science, Inc.	$100.00	$78.43	$29.41	$31.84	$20.31	$35.69
NASDAQ Composite Index	$100.00	$98.20	$113.82	$157.44	$178.53	$188.75
NASDAQ Biotechnology Index	$100.00	$111.81	$147.48	$244.24	$327.52	$364.93

The stock price performance included in this graph is not necessarily indicative of future stock price performance.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

We did not repurchase any of our equity securities during the year ended December 31, 2015.

Item 6. Selected Financial Data

The following selected consolidated financial data should be read in conjunction with Part II, Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations," and our Consolidated Financial Statements and the accompanying notes included in Part II, Item 8, "Financial Statements and Supplementary Data" of this Annual Report on Form 10-K.

Table of Contents

The Consolidated Statements of Operations data for each of the years ended December 31, 2015, 2014, and 2013 and the Consolidated Balance Sheets data as of December 31, 2015 and 2014 are derived from our audited Consolidated Financial Statements included in Part II, Item 8, "Financial Statements and Supplementary Data" of this Annual Report on Form 10-K. The Consolidated Statements of Operations data for the years ended December 31, 2012 and 2011 and the Consolidated Balance Sheets data as of December 31, 2013, 2012, and 2011 are derived from our audited Consolidated Financial Statements that are not included in this Annual Report on Form 10-K. Our historical results are not necessarily indicative of our results in any future period.

	Year Ended December 31,				
	2015	2014	2013	2012	2011
	($ in thousands, except per share data)				
Consolidated Statements of Operations data:					
Total revenue	$492	$180	$200	$153	$—
Total cost of revenue	722	2,312	7,501	7,804	13
Research and development expenses (1)	25,892	17,735	13,762	10,193	7,171
Selling, general and administrative expenses (1)	11,285	10,087	9,440	11,546	12,795
Warrant revaluation and other finance income (expense)	2,929	3,930	(1,053)	20,404	2,562
Loss from continuing operations	(34,453)	(25,650)	(31,554)	(13,143)	(23,931)
Net loss	(34,453)	(25,650)	(31,554)	(12,687)	(24,025)
Per Share Information (2):					
Loss from continuing operations per common share - basic	$(0.82)	$(0.63)	$(1.06)	$(1.47)	$(10.91)
Loss from continuing operations per common share - diluted	$(0.85)	$(0.70)	$(1.12)	$(2.65)	$(10.99)
Net loss per common share - basic	$(0.82)	$(0.63)	$(1.06)	$(1.42)	$(10.96)
Net loss per common share - diluted	$(0.85)	$(0.70)	$(1.12)	$(2.60)	$(11.04)

(1) Included in both selling, general and administrative expenses and research and development expenses, combined, is $2.0 million, $1.2 million, $1.2 million, $1.2 million, and $2.9 million of stock-based compensation for the years ended December 31, 2015, 2014, 2013, 2012, and 2011, respectively.

(2) The per share data has been retroactively adjusted to reflect the April 30, 2013 reverse stock split of 25 to 1. See Note 13 of the Consolidated Financial Statements for a description of our computation of basic and diluted loss per share attributable to common stockholders.

	As of December 31,				
	2015	2014	2013	2012	2011
	($ in thousands)				
Consolidated Balance Sheets Data:					
Cash and cash equivalents	$29,268	$37,495	$60,033	$31,346	$10,799
Total current assets	30,994	39,349	61,860	33,156	12,499
Total assets	36,712	45,634	69,014	40,603	20,274
Total current liabilities	15,365	3,493	3,593	1,554	9,611
Warrant liability, current and long term	8,275	11,286	15,216	14,515	23,754
Total liabilities	22,509	15,225	19,348	16,413	36,541
Total equity (deficit) and noncontrolling interest	14,203	30,409	49,666	24,190	(16,268)

We have never paid dividends on our common stock.

Table of Contents

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

This Management's Discussion and Analysis of Financial Conditions and Results of Operations should be read in conjunction with our financial statements and the related notes included elsewhere in this Form 10-K.

Overview

We are an autologous cell and gene therapy company translating personalized biologics into medical breakthroughs. We are focused on discovering and developing new therapies for the localized treatment of diseases affecting the skin, connective tissue and joints. Our approach to personalized biologics is distinctive based on our proprietary autologous fibroblast technology: targeting the underlying cause of disease by using cells from the skin to create localized therapies—with or without genetic modification—that are compatible with the unique biology of each patient.

Development Programs

Our most advanced development program is azficel-T for vocal cord scarring resulting in chronic or severe dysphonia. We are currently in a Phase II clinical trial for this indication. We have completed dosing in this trial and expect to announce primary endpoint results in the second quarter of 2016.

In collaboration with Intrexon, we are in pre-clinical development with two gene-therapy product candidates. Our lead gene-therapy product candidate, FCX-007, has received orphan drug designation as well as rare pediatric disease
designation from the FDA and is in late-stage pre-clinical development for the treatment of RDEB, a devastating, rare, congenital, painful, progressive. blistering skin disease that typically leads to premature death. We expect to file an amended IND with the FDA and, subject to FDA approval, initiate our phase I/II clinical trial in the second quarter of 2016. We are also in pre-clinical development of our second gene-therapy product candidate, FCX-013, for the treatment of linear scleroderma, an excess production of extracellular matrix characterized by skin fibrosis and linear scars. We have completed our proof-of-concept study for FCX-013 and expect to file an IND in 2017. We plan to seek orphan drug designation for FCX-013.

In September 2015, we and Intrexon entered into a letter of agreement pursuant to which we mutually agreed to terminate our collaboration with respect to the development of potential therapies to treat Ehlers-Danlos Syndrome (hypermobility type) due to technical hurdles. As a result, we no longer have any rights or obligations under the 2012 ECC with respect to the development of "autologous human fibroblasts genetically modified to express bioactive Tenascin-X locally to correct connective tissue disorders".

In December 2015, we expanded our collaboration with Intrexon to pursue the research, development and commercialization of products for the treatment of chronic inflammation and degenerative diseases of human joints through intra-articular or other local administration of genetically modified fibroblasts. We are currently in the research phase for a gene therapy to treat arthritis under this collaboration. Our goal is to deliver a protein therapy locally to the joint to provide sustained efficacy while avoiding key side effects typically associated with systemic therapy.

We also have a scientific research collaboration with UCLA focused on media that promotes genomic stability in induced pluripotent stem cell cultures. We had previously been a party to additional collaborations with UCLA and the Massachusetts Institute of Technology relating to isolating stem cell sub-populations in the skin; however, we terminated these other programs and related agreements in 2015.

Commercial Programs

LAVIV (azficel-T) is an FDA-approved biological product that uses our proprietary autologous fibroblast technology for the improvement of the appearance of moderate to severe nasolabial fold wrinkles in adults. In 2013, we shifted

our strategic focus to diseases affecting the skin, connective tissue and joints, resulting in the pre-clinical and clinical product candidates mentioned above. As a result, we no longer actively market or promote LAVIV to physicians but will continue to accept prescriptions, for which we expect a nominal amount in 2016.

See Part I, Item 1, "Business" of this Annual Report on Form 10-K for additional details regarding our development programs, commercial programs, and collaboration agreements.

Critical Accounting Policies

The following discussion and analysis of financial condition and results of operations are based upon our Consolidated Financial Statements, which have been prepared in conformity with U.S. generally accepted accounting principles (“GAAP”).

Table of Contents

Preparing financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses. Estimates are based on our historical operations, our future business plans and projected financial results, the terms of existing contracts, our observance of trends in the industry, information provided by our customers and information available from other outside sources, as appropriate. These estimates and assumptions are affected by the application of our accounting policies. Critical accounting policies and practices are both important to the portrayal of a company's financial condition and results of operations, and require management's most difficult, subjective or complex judgments, often as a result of the need to make estimates about the effects of matters that are inherently uncertain. Actual results could differ from such estimates due to changes in economic factors or other conditions that are outside the control of management. A summary of our significant accounting policies is described in Note 3 of the Consolidated Financial Statements contained in this Form 10-K.

Basis of Presentation

The following discussion should be read in conjunction with the Consolidated Financial Statements and the accompanying Notes of the Consolidated Financial Statements included in this Form 10-K.

The prior year financial data included in Part II, Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations," contains certain reclassifications to the results of operations for the years ended December 31, 2014 and 2013 to conform to the presentation for the year ended December 31, 2015 in this Form 10-K. These reclassifications were made in conjunction with the Company's strategic shift away from the aesthetics market (LAVIV) and towards diseases affecting the skin, connective tissue and joints. See Note 2 of the Consolidated Financial Statements included in this Form 10-K for additional details.

Results of Operations

Comparison of Years Ending December 31, 2015, 2014 and 2013

Revenue and Cost of Revenue

Revenue and cost of revenue were comprised of the following:

	Year Ended December 31,			2015 vs 2014		2014 vs 2013	
($ in thousands)	2015	2014	2013	% Change		% Change	
Revenue from product sales	$270	$170	$200	58.8	%	(15.0)	% (1)
Collaboration revenue	222	10	—	2,120.0	%	100.0	% (2)
Total revenue							