Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration Statement No. 333-1995588

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities became effective under the Securities Act of 1933, as amended. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting an offer to buy these securities, in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED FEBRUARY 4, 2015

PRELIMINARY PROSPECTUS SUPPLEMENT
(To the Prospectus dated May 9, 2014)

Shares

AXOGEN, INC.

Common Shares

We are offering of our common shares, par value $0.01 per share, pursuant to this prospectus supplement and the accompanying prospectus.

Our common shares trade on the NASDAQ Capital Market under the symbol "AXGN." On February 3, 2015, the last reported sale price of our common shares on the NASDAQ Capital Market was $3.39 per share.

The aggregate market value of our outstanding common shares held by non-affiliates, or public float, pursuant to General Instruction I.B.6 of Form S-3 was approximately $68.69 million based on 19,488,814 shares of outstanding common shares, of which 2,734,374 shares were held by affiliates, and a price of $4.10 per share, which was the last reported sale price of our common shares on the NASDAQ Capital Market on January 8, 2015. Other than the common shares offered pursuant to this prospectus supplement, and the prospectus supplements dated November 12, 2014 in connection with our registered offerings of the common shares at an aggregate offering price of $1.749 million and $3.55 million, respectively, we have not offered any securities pursuant to General Instruction I.B.6 of Form S-3 during the prior 12 calendar month period that ends on and includes the date of this prospectus supplement. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities registered on this registration statement in a public primary offering with a value exceeding more than one-third of our public float in any 12-month period so long as our public float remains below $75.0 million.

Investing in our securities involves a high degree of risk. You should carefully review and consider the risks and uncertainties described under the heading "Risk Factors" beginning on page S-8 of this prospectus supplement and on page 3 of the accompanying prospectus.

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

	Per Share	Total
Public offering price	$	$
Underwriting discount(1)	$	$
Proceeds, before expenses, to us	$	$

(1) In addition, we have agreed to reimburse the underwriter for certain expenses. See "Underwriting" on page S-26 of this prospectus supplement for additional information.

We have granted a 30-day option to the underwriter to purchase up to additional common shares solely to cover over-allotments, if any.

The underwriter expects to deliver the shares offered hereby against payment therefor on or about February , 2015.

Wedbush PacGrow Life Sciences

February , 2015

TABLE OF CONTENTS

PROSPECTUS SUPPLEMENT

PROSPECTUS

ABOUT THIS PROSPECTUS SUPPLEMENT

This document contains two parts. The first part is this prospectus supplement, which describes the terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated May 9, 2014, including the documents incorporated by reference therein, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission (the "SEC"), before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date, for example, a document incorporated by reference in the accompanying prospectus, the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information contained in or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not, and the underwriter has not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriter is not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled "Where You Can Find More Information" and "Incorporation of Certain Documents by Reference."

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

All references in this prospectus supplement and the accompanying prospectus to "AxoGen," the "Company," "we," "us," "our," or similar references refer to AxoGen, Inc. and its subsidiaries, except where the context otherwise requires or as otherwise indicated.

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

Table of Contents

NOTE ON FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents the Company has filed with the SEC that are incorporated by reference in this prospectus supplement or the accompanying prospectus contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These forward-looking statements may concern possible or anticipated future results of operations or business developments. These statements are based on management's current expectations or predictions of future conditions, events or results based on various assumptions and management's estimates of trends and economic factors in the markets in which we are active, as well as our business plans. Words such as "expects", "anticipates", "intends", "plans", "believes", "seeks", "estimates", "projects", "forecasts", "may", "should", variations of such words and similar expressions are intended to identify such forward-looking statements. The forward-looking statements may include, without limitation, statements regarding product development, product potential, regulatory environment, sales and marketing strategies, capital resources, operating performance, the preliminary unaudited financial results for the fourth quarter of 2014 and the year ended December 31, 2014, the estimated timing of final reports of financial results for the year ended December 31, 2014 or the closing of this offering. The forward-looking statements are subject to risks and uncertainties, which may cause results to differ materially from those set forth in the statements. Forward-looking statements should be evaluated together with the many uncertainties that affect the Company's business and its market, particularly those discussed in the risk factors and cautionary statements in the Company's filings with the SEC, including as described in "Risk Factors" contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, and in our most recent Annual Report on Form 10-K, as well as any amendments thereto reflected in subsequent filings with the SEC.

Forward-looking statements are not guarantees of future performance, and actual results may differ materially from those projected. The forward-looking statements are representative only as of the date they are made, and the Company assumes no responsibility to update any forward-looking statements except as required by law.

This prospectus supplement contains estimates, projections and other statistical data made by independent parties and by us relating to market size and growth, the incidence of certain medical conditions and other industry data. These data, to the extent they contain estimates or projections, involve a number of subjective assumptions and limitations, and you are cautioned not to give undue weight to such estimates or projections. Industry publications and other reports we have obtained from independent parties generally state that the data contained in these publications or other reports have been obtained in good faith or from sources considered to be reliable, but they do not guarantee the accuracy or completeness of such data. While we believe that the data from these industry publications and other reports are generally reliable, we have not independently verified the accuracy or completeness of such data. These and other factors could cause results to differ materially from those expressed in these publications and reports.

We have provided estimates of the potential United States market for our products. These estimates are based on a number of factors, including our expectation as to the number of patients with a certain medical condition that would potentially benefit from a particular product. While we have determined these estimates based on assumptions that we believe are reasonable, there are a number of factors that could cause our expectations to change or not be realized. Among these factors are the following: there is no assurance that doctors will adopt the use of our products as quickly or as broadly as we have assumed or that the number of peripheral nerve injuries that can be repaired with products is as large as we estimate. It is possible that the ultimate market for our products will differ significantly from our expectations due to these or other factors. As a result of these and other factors, investors should not place undue reliance on such estimates.

Table of Contents

SUMMARY

This summary is not complete and does not contain all the information that you should consider before investing in our common stock. Before making an investment decision, you should carefully read the entire prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein, including the risk factors described in "Risk Factors" beginning on page S-8 of this prospectus supplement, as well as the financial statements and related notes and the other information incorporated by reference herein.

Company Overview

General

We are a leading medical technology company dedicated to peripheral nerve repair. Peripheral nerves provide the pathways for both motor and sensory signals throughout the body and their damage can result in the loss of muscle function and/or feeling.

Nerves can be damaged in a number of ways. When a nerve is cut due to a traumatic injury or surgery, functionality of the nerve may be compromised, causing the nerve to no longer carry the signals to and from the brain to the muscles and skin. This type of injury generally requires a surgical repair. The traditional gold standard has been to either suture the nerve ends together directly without tension or to bridge the gap between the nerve ends with a less important nerve surgically removed from elsewhere in the patient's own body referred to as nerve autograft. In addition, compression on a nerve or blunt force trauma can cause nerve injuries that may require surgical intervention.

In order to improve the options available for the surgical repair and regeneration of peripheral nerves, we have developed and licensed patented and patent pending regenerative medicine technologies. Our innovative approach to regenerative medicine has resulted in first-in-class products that we believe are redefining the peripheral nerve repair market. Our products offer a full suite of surgical nerve repair solutions including Avance® Nerve Graft, the only off-the-shelf commercially available processed nerve allograft, human nerve tissue obtained from a donor, known to us to be available for bridging severed nerves without the comorbidities associated with a nerve autograft second surgical site, such as loss of feeling where the nerve was removed and potential pain at the donor site. Our AxoGuard® line of products are a porcine submucosa extracellular matrix, or ECM. AxoGuard® Nerve Connector is a coaptation aid to facilitate the tensionless repair of severed nerves, and AxoGuard® Nerve Protector is used to wrap and protect injured peripheral nerves and reinforce the nerve reconstruction while preventing soft tissue attachments.

Our products are used by surgeons during surgical interventions to repair a wide variety of nerve injuries throughout the body. These injuries range from a simple laceration of a finger to a complex brachial plexus injury (an injury to the network of nerves that originate in the neck) as well as nerve injuries caused by dental and other surgical procedures. Avance® Nerve Graft provides surgeons bridging material with the micro-architecture of a human nerve. This structure is essential and allows for bridging nerve gaps or discontinuities up to 70mm in length. Additionally, Avance® Nerve Graft has product and sales synergies with AxoGuard® Nerve Protector and AxoGuard® Nerve Connector. AxoGuard® products provide the unique features of pliability, suturability, and translucence for visualization of the underlying nerve, while also allowing the patient's own cells to incorporate into the extracellular matrix to remodel and form a tissue similar to the outermost layer of the nerve (nerve epineurium).

We have reported a net loss of approximately $14,557,000 and $9,418,000 for the years ended December 31, 2013 and 2012, respectively, and a net loss of approximately $11,219,000 and $10,448,000 for the nine months ended September 30, 2014 and 2013, respectively.

We were incorporated under the laws of Minnesota in 1977. Our principal executive offices are located at 13631 Progress Boulevard, Suite 400, Alachua, Florida 32615 and our telephone number is (386) 462-6800. Our website address is www.axogeninc.com. We have included our website address in this prospectus supplement solely as an inactive textual reference. The information contained on, or that can be accessed through, our website is not part of this prospectus supplement.

Peripheral Nerve Regeneration Market Overview

Peripheral nerve injury ("PNI") is a major source of disability impairing the ability to move muscles or to feel normal sensations. Failure to treat nerve damage can, in severe cases, lead to full loss of sensation and/or function, pain and, sometimes, amputation. Many peripheral nerve injury patients who receive treatment do not optimally recover. Patients may suffer from both reduced, or no, muscle strength, and reduced, or no, sensitivity and pain.

Table of Contents

Every day patients suffer traumatic wounds to peripheral nerves severe enough to require surgical treatment, including injuries from motor vehicle accidents, collisions, gun wounds, dislocations, fractures, lacerations, or other forms of penetrating trauma. The peripheral nerves commonly injured from these traumas include the digital, median, ulnar, radial, facial, spinal accessory and brachial plexus nerves. Traumatic PNI described herein, and excluding Oral and Carpal Tunnel defined below, is referred to by us as occurring in the "Extremity" PNI market.

Based upon epidemiological studies regarding the number of trauma patients and incidence of peripheral nerve injury in the population, we believe that each year in the U.S. more than 1.4 million people suffer traumatic injuries to peripheral nerves. We estimate that that traumatic and non-traumatic injuries to peripheral nerves result in over 700,000 extremity nerve repair procedures in the U.S. annually. ("Health", United States, 2011, Publication of U.S. Department of Health & Human Services; Noble, et al. J of Trauma Injury Infection and Critical Care 1998).

Beyond traumatic injury to nerves, nerve damage also occurs due to surgical intervention and represents an opportunity for surgical repair. Some of these nerve cases PNIs can also occur during certain dental and oral surgery procedures such as third molar extractions, and placement of dental implants and removal of tumors during which an injury may be caused to one or more sections of the trigeminal nerve ("Oral"). This can result in numbness in certain areas of the face and mouth. Finally, nerves are also damaged or compromised due to compression injuries. For instance, severe and recurrent carpal tunnel cases may result in complications and damage to the nerve that requires further surgical intervention and protection of the nerve. We refer to PNI caused by carpal tunnel syndrome as "Carpal Tunnel". In addition, nerves can be severed during the removal of cancerous tissues. For example, nerves that support erectile function may be injured or

removed following a surgical prostatectomy to remove prostate cancer resulting in impotence and incontinence. Further, breast cancer patients may have reduced sensation in the tissue used to reconstruct the breast after mastectomy.

In the cases where a nerve is severed, if the gap between the two ends of the nerve is extremely small, the surgeon may be able to reconnect the nerve without tension through direct suturing or for gaps up to a few millimeters in length, using a coaptation aid ("Primary Repair"). When the gap in the nerve tissue is more than a few millimeters in length, the surgeon typically needs to bridge the gap between the nerve ends to ensure a tension-free repair ("Gap Repair"). Historically, to repair a gap in a severed nerve, surgeons have relied on a nerve autotransplantation (autologous nerve grafting or nerve autograft). In nerve autograft procedures, surgeons remove nerve from another part of the patient's body, frequently the sural nerve from the back of the lower leg, to repair the damaged nerve. Nerve autografting is often effective in repairing a damaged peripheral nerve, but it presents a tradeoff — the surgeon can attempt to fix the damaged nerve but must create an additional nerve deficit at another location in the body. For example, a patient may opt to get movement and feeling back in their finger while losing some sensation in their foot. Additionally, the secondary surgery to obtain the needed nerve autograft also increases operating time, and thus medical expenses, and increases the risk of surgical site infection and other complications. In the case of extreme trauma where multiple nerves need to be repaired, it may not be possible to recover enough nerve from the patient to complete the Gap Repair. Further, nerve autograft tissue may not provide an appropriate diameter match with the diameter of the injured nerve stump, an important factor in a successful repair outcome.

Drawbacks of repair with autograft nerve eventually led to the development of hollow-tubes conduits, or hollow-tube nerve cuffs for peripheral nerve Primary and Gap Repair made of, for instance, bovine collagen or polyglycolic acid. The nerve cuff is typically an absorbable hollow tube that, unlike natural peripheral nerve, does not have internal microarchitecture and endoneurial tubes to support regenerating axons; as a result, it is deficient in the qualities that natural nerve possesses to support nerve regeneration across a gap. Hollow-tube conduits may also lack pliability and structural integrity needed when used around joints and may be difficult to use in a confined space. Clinical data has demonstrated that hollow-tube conduits are most effective only when used in very short gaps, what we define as Primary Repair, and the reliability of successful nerve recovery diminishes as gap length increases.

The shortcomings of hollow-tube conduits for nerve repair limit where they may be used effectively. Thus, we believe the nerve repair market needs an alternative off-the-shelf product that provides the natural ECM scaffold and three-dimensional structure of a typical nerve for bridging nerve discontinuities without the comorbidities of an additional second surgical site required for harvest of autograft nerve tissue. We believe our Avance® Nerve Graft and AxoGuard® Nerve Connector products meet this market need.

Compression on a nerve or blunt force trauma can also cause nerve injuries that may require surgical intervention. In these cases, the nerve is not severed and thus does not create the need for a Primary or Gap Repair. However, the surgeon may want to protect and isolate the nerve during the healing process. In these situations nerve protection is provided by wrapping the nerve with a particular material ("Nerve Protection").

AxoGuard® Nerve Protector is a porcine submucosa extracellular matrix used for Nerve Protection. Other Nerve Protection products are usually made from bovine collagen or polyglycolic acid and are typically absorbable. AxoGuard® Protector provides the

Table of Contents

unique features of pliability, suturability, and translucence for visualization of the underlying nerve, while also allowing the patient's own cells to incorporate into the extracellular matrix to remodel and separate the nerve from the surrounding tissue layers. One of the advantages of AxoGuard® Nerve Connector is that it reduces the number of required sutures (versus direct repair), and we believe it can also reduce surgery time by up to 40%. (Boechstyns, Jhand Surg. 2013;38:2405-2411).

Based on estimates prepared by us, we believe the annual U.S. PNI market for our current product portfolio for Extremity, Oral and Carpal Tunnel is approximately $1.6 billion (the "Market"). We estimate that the Extremity portion of the Market is approximately $1.3 billion. The estimated size of the Extremity portion of the Market is based upon epidemiological studies regarding the general number of trauma patients, physician interviews and incidence of PNI in the population. We believe that, each year in the U.S., more than 1.4 million people suffer traumatic injuries to peripheral nerves. We estimate that traumatic and non-traumatic injuries to peripheral nerves result in over 700,000 Extremity nerve repair procedures. ("Health", United States, 2011, Publication of U.S. Department of Health & Human Services; Noble, et al. J of Trauma Injury Infection and Critical Care 1998; Kurt Brattain, MD, Magellan Medical Technology Consultants, Inc., Minneapolis, Minnesota 2013). We further estimated the portion of extremity nerve repair procedures that would be addressed by our Gap Repair, Primary Repair and Nerve Protection products then applied the average sales price of the AxoGen product that applies to the procedure (Avance® Nerve Graft, AxoGuard® Nerve Connector and AxoGuard® Nerve Protector, respectively). As a result, we estimate that the market sizes, within the Extremity portion of the Market, for our Avance® Nerve Graft, AxoGuard® Nerve Connector and AxoGuard® Nerve Protector products are approximately $668 million, $161 million and $483 million, respectively.

We estimate that the Oral portion of the Market is approximately $129 million, based upon research that has indicated approximately 68,000 PNI occur in the U.S. each year that are related to third molar extractions, anesthetic injections and dental implants. (The Prophylactic Extraction of Third Molars: A Public Health Hazard: Jay W. Friedman, DDS, Health Policy and Ethics; Peer Reviewed; Friedman American Journal of Public Health; September 2007, Vol 97, No. 9, pp 1554 — 1559 — Journal of Oral Implantology, Vol. XXXVI/No. Five/2010; "Inferior Alveolar Nerve Injury in Implant Dentistry: Diagnosis, Causes, Prevention, and Management"; Ahmed Ali Alhassani, BDS - "Nerve Injuries after Dental Injection: A Review of the Literature"; Clinical Practice, July/August 2006, Vol. 72, No. 6, Miller H. Smith, BMedSc, DDS; Kevin E. Lung, BSc, DDS, MSc, FRCD(C)). We have applied the average sales price of the Avance® Nerve Graft and AxoGuard® Nerve Protector that address Oral PNI in order to derive the Oral portion of the Market.

We estimate that the Carpal Tunnel portion of the Market is approximately $160 million. According to literature, there are approximately 500,000 carpal tunnel relief surgeries performed annually in the U.S., and, we assume that 20% of such surgeries require

revision procedures to address the recurrence of symptoms. ("Vein-Graft Wrapping for the Treatment of Recurrent Compression of the Median Nerve", Microsurgery 16:752-756 1995, Dean G. Sotereanos, M.D.). As a result, we estimate that approximately 100,000 carpal tunnel revision surgeries are performed each year in the U.S. to address the recurrence of symptoms. These revision surgeries are required due to compression of the nerve due to soft tissue attachments from the surrounding tissue or tissue infiltration entrapping the nerve. To prevent additional recurrences, surgeons will opt to use a Nerve Protection product, such as the AxoGuard® Nerve Protector. In order to derive the Carpal Tunnel portion of the Market, we multiplied the average sales price of our AxoGuard® Nerve Protector by the number of estimated carpal tunnel revisions.

We continue to look at expansion markets beyond those that we have defined as Extremity, Oral and Carpal Tunnel. In addition to these areas, we believe a market exists to treat nerves that are severed during the removal of both benign and cancerous tumors. For example, nerves that support erectile function may be injured or removed following a surgical prostatectomy to remove prostate cancer, resulting in impotence and incontinence. Further, a patient who receives repair of peripheral nerves in the breast following a mastectomy and reconstruction may avoid the reduced sensation typically experienced by many breast cancer patients. We believe that we will continue to identify market expansion opportunities for our current product portfolio.

Table of Contents

AxoGen Clinical Trials

Generating clinical data is an important component of our marketing strategy. We are currently performing three clinical studies to gather data on the Avance® Nerve Graft. The studies are "A Multicenter Retrospective Study of Avance® Nerve Graft Utilization, Evaluations and Outcomes in Peripheral Nerve Injury Repair ("RANGER®")", "A Multicenter, Prospective, Randomized, Comparative Study of Hollow Nerve Conduit and Avance® Nerve Graft Evaluation Recovery Outcomes of the Nerve Repair in the Hand ("CHANGE")" and a pilot study to evaluate the use of Avance® Nerve Graft in the reconstruction of nerves following prostatectomy.

We will continue to accept patients in the RANGER® clinical study, a utilization registry of Avance® Nerve Graft. Two publications and 35 scientific conference presentations have been generated to date from the registry.The RANGER® Study is an observational study in current enrollment. It is designed to allow enrollment of up to a total of 1,000 subjects over the next several years. The follow-up for the RANGER® Study is standard of care up to 36 months post nerve repair. At the time of our Biologics License Application ("BLA") submission for Avance® Nerve Graft, if 1,000 subjects have not been enrolled and follow-up completed, we will submit an interim report in the BLA for the enrolled subjects.

We have worked with leading institutions, researchers and surgeons to support innovation in the field of surgical peripheral nerve repair. We believe to date, RANGER® is the largest multi-center observational clinical study conducted in peripheral nerve gap repair. Our upcoming RECON study will also continue our clinical work, providing a new multi-center, prospective, randomized, clinical study on the Avance® Nerve Graft. The January 2012 edition of Microsurgery and November 2012 edition of The Journal of Hand Surgery each contain an article summarizing RANGER® study results. The article in the January 2012 edition of Microsurgery reported on 55 Avance® Nerve Graft nerve repairs and resulted in meaningful motor and sensory recovery in 87% of nerve discontinuities between 5 and 50 mm. Additionally, no implant related adverse events have been reported. (Brooks, et al. 2012). Processed nerve allografts for peripheral nerve reconstruction: A multicenter study of utilization and outcomes in sensory, mixed, and motor nerve reconstructions. Microsurgery, 32: 1—14. doi: 10.1002/micr.20975 and Cho, et al. 2012, J Hand Surg Am 37(11):2340-9). In Cho et al., RANGER® showed the Avance® Nerve Graft to provide 89% meaningful recovery for nerve injuries, and 78% meaningful recovery for mixed and motor nerve injuries. An expanded data milestone was presented at the 5th Vienna Symposium on Surgery of Peripheral Nerves in March 2014 and such expanded RANGER® data provides that of the injuries repaired with the Avance® Nerve Graft 90%, 80% and 87% achieved meaningful recovery for gap lengths of 5-14 mm, 15-29 mm and 30-65 mm, respectively.

The following describes available clinical outcomes data from published papers on the leading synthetic and collagen conduit. We have not performed a head-to-head clinical study comparing the Avance® Nerve Graft to the leading synthetic and collagen conduit. Published papers on the leading synthetic collagen conduit by Weber, et al., 2000 and Wangensteen and Kalliainen, 2009, showed meaningful improvement: 74% in sensory nerves and 43% in sensory, mixed and motor nerves, respectively, of cases bridging a gap in the particular type of nerve. A paper published by Haug, et al., 2013 on the leading synthetic and collagen conduit showed meaningful improvement in 40% sensory nerves using the static 2-point discrimination test. Autograft studies where autograft and direct repair or direct suture were tested by Weber, et al., 2000, Kim and Kline 2001-2006, Frykman and Gramyk, 1991, Frykman and Gramyk, 1991 and Kallio, 1993, as interpreted by Brooks et al. 2012, reported meaningful recovery: 86% in sensory nerves, 67-86% in sensory and mixed nerves, 80% in sensory nerves, 75-78% mixed nerves and 70% sensory nerves, respectively, of cases bridging a gap in the particular type of nerve. Published papers by Kim and Kline 2001-2006 and Frykman and Gramyk, 1991 reported successful recovery in 75% and 78% of mixed and motor nerves, respectively. A study by Kallio et al., 1993 showed recovery in 67% of mixed and motor nerves where recovery was defined as results indicating a classification of useful or better motor and sensory recovery.

We conducted the CHANGE study as a pilot comparative study. It is a multicenter prospective randomized comparative pilot study of hollow tube conduits and Avance® Nerve Graft. Subject enrollment and follow-up have been completed and report development is in process. A pilot study on the repair of the cavernous nerves in prostate cancer patients at Vanderbilt has completed enrollment and a 24 month follow-up. The post nerve repair data analysis and report development are in process for this study and should be available the first half of 2015. A case series in digital nerve repair from the Mayo Clinic in Rochester MN has already been published. In addition, a number of investigator initiated studies and publications have been completed.

U.S. Government Regulations Overview

As previously disclosed, the U.S. Food and Drug Administration (the "FDA") issued a letter to us in November 2010 stating the

agency's intent to exercise enforcement discretion with respect to the introduction or delivery for introduction into interstate commerce of the Avance® Nerve Graft assuming that certain conditions are met relating to the transition of the Avance® Nerve Graft to regulation as a biological product under section 351 of the Public Health Service Act (the "PHS Act"). FDA is permitting the product to be distributed, subject to FDA enforcement discretion, provided that we: (1) transition to compliance with section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act, the current good manufacturing practice regulations in 21 CFR Parts 210 and 211 and the applicable regulations and standards in 21 CFR Parts 600-610 prior to initiation of a phase 3 clinical trial designed to demonstrate the safety, purity, and potency of the Avance® Nerve Graft; (2) conduct a phase 3 clinical trial to demonstrate safety, purity and potency of the Avance® Nerve Graft under a Special Protocol Assessment ("SPA"); (3) continue to comply with the regulations and standard at 21 CFR Part 1271; and (4) exercise due diligence in executing the transition plan.

Table of Contents

With regard to the phase 3 clinical trial in the foregoing condition (2), we and the FDA agreed to the SPA in August 2011 and in accordance with FDA regulations, 21 CFR Part 312, we submitted an Investigational New Drug Application ("IND") to the FDA in April 2013. We are currently responding to FDA comments regarding the IND, which is not yet effective. We expect enrollment of patients into the phase 3 clinical trial to begin in the later part of 2015. On June 7, 2013, the FDA placed the IND on Clinical Hold, pending the FDA's receipt of additional information relating to the potency, mechanical characterization, and labeling of the product. The phase 3 clinical trial cannot begin until the FDA lifts the Clinical Hold. We are developing the data and information to respond to the FDA's requests. Additionally, we were audited by the FDA in March 2013 and the quality system was found to be in compliance with 21 CFR Part 1271. We are working to ensure compliance with the applicable regulations by having ongoing discussions on the transition of the quality system to 21 CFR Parts 210/211 and 600-610 regulations with the FDA and being audited by the FDA for compliance to 21 CFR Part1271 of the regulations. Final determination of regulatory compliance will be made during FDA's pre-license inspection as part of the BLA review. If FDA is unable to agree with us, or if we are unable to meet the standards required of it by the FDA, regarding preclinical studies, clinical studies and Chemistry, Manufacturing, and Controls, the approval of our BLA would become impossible or delayed.

The FDA will end the period of enforcement discretion upon a final determination of our BLA submission or if the FDA finds that we do not meet the conditions for the transition plan, or are not exercising due diligence in executing the transition (e.g., not progressing toward the IND submission, study completion, or BLA submission in a timely or adequate fashion). If final action on the BLA is negative or we are found to not meet the conditions for the transition plan or its execution, we will not be able to continue to distribute the Avance® Nerve Graft, and our business and financial condition will be materially adversely affected.

We continue to work diligently with the FDA and, in this context, continue to distribute the Avance® Nerve Graft products.

Recent Developments

Preliminary Unaudited Financial Results

On February 4, 2015, we issued a press release announcing our preliminary unaudited revenue and certain other financial information for the fourth quarter and full year ended December 31, 2014.

We expect fourth quarter revenue of approximately $4.79 million, a 61% increase compared to revenue of approximately $2.98 million in the fourth quarter of 2013. For the full year ended December 31, 2014, revenue is expected to be approximately $16.8 million, representing a 54% increase compared to revenue of approximately $10.9 million for the full year ended December 31, 2013.

In addition to these announced results, as of December 31, 2014, we had cash and cash equivalents of approximately $8.2 million, which reflects the impact of approximately $0.9 million of financing expenses paid for a refinancing completed in November 2014, under which (i) we borrowed $25 million under a term loan agreement (the "Three Peaks Term Loan Agreement") dated November 12, 2014, by and among us, as borrower, our wholly owned subsidiary AxoGen Corporation, as guarantor, the lenders party thereto and Three Peaks Capital S.a.r.l., an indirect wholly-owned subsidiary of Oberland Capital Healthcare Master Fund LP, as administrative and collateral agent for the lenders, and (ii) we terminated the Revenue Interests Purchase Agreement by and between us and PDL BioPharma, Inc. ("PDL") dated October 5, 2012. The Three Peaks Term Loan Agreement is secured by substantially all of our tangible and intangible assets (including, without limitation, our intellectual property).

As of January 2, 2015, we had outstanding 19,488,814 shares of common stock, and common stock and common stock equivalents totaled 22,419,312 shares.

These preliminary results are based on currently available financial and operating information and management's preliminary analysis of the unaudited financial results for the quarter and year ended December 31, 2014 and are subject to finalization in connection with the preparation of our audited financial statements for the year ended December 31, 2014. We have not completed the preparation of our financial statements for the year ended December 31, 2014 and additional details with respect to our 2014 results of operations are not yet available. We currently intend to report our complete financial results for the full year ended December 31, 2014 in early March 2015.

Table of Contents

Expansion of AxoGen Sales Team

We provide full sales and distribution services through both a direct sales force and a team of independent distributors. As of December 31, 2014, we had 29 direct sales professionals and 23 independent distributors. We provide support and resources for independent distributors both within and outside the United States and are increasing our direct sales force in selected United States territories.

Table of Contents

THE OFFERING

Common shares offered by us	common shares
Over-allotment option	We have granted the underwriter an option to purchase up to additional shares of common stock from us at the public offering price set forth on the cover page of this prospectus supplement, less the underwriting discounts and commissions, at any time and from time to time during the 30-day period from the date of this prospectus supplement to cover over-allotments, if any.
Common shares to be outstanding immediately after this offering	common shares
Use of Proceeds	We intend to use the net proceeds of this offering for continued expansion of sales force and surgeon education and general corporate purposes. Our management will retain broad discretion over the allocation of the net proceeds from the sale of the common shares. See "Use of Proceeds" on page S-23 for more information.
Insider Participation	Certain of our directors and officers have indicated an interest in purchasing up to an aggregate of approximately $75,000 common shares in this offering at the public offering price. Because this indication of interest is not a binding agreement or commitment to purchase, these directors and officers may elect not to purchase any shares in this offering, or the underwriter may elect not to sell any shares in this offering to them.
Risk Factors	Before purchasing shares of our common stock, you should carefully consider the risk factors described in "Risk Factors" beginning on page S-8 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.
NASDAQ Capital Market Symbol	Our common shares are traded on the NASDAQ Capital Market under the symbol "AXGN".

Except as otherwise indicated, all information in this prospectus supplement is based on 19,488,814 shares outstanding on February 2, 2015, assumes no exercise by the underwriter of its over-allotment option to purchase up to an additional shares to cover over-allotments, if any, and excludes:

- 2,889,310 common shares issuable upon the exercise of options outstanding as of February 2, 2015 at a weighted average exercise price of $3.06 per share;
- 89,686 common shares issuable upon the exercise of warrants outstanding as of February 2, 2015 at an exercise price of $2.23 per share; and
- 317,187 additional common shares reserved for future issuance as of February 2, 2015 under our 2010 Stock Incentive Plan.

Unless otherwise indicated, all information in this prospectus assumes no exercise of the outstanding options or the warrants described above.

Table of Contents

RISK FACTORS

An investment in our common shares involves a high degree of risk. Before deciding whether to invest in our common shares, you should consider carefully the risk factors described below, in conjunction with this entire prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement. In particular, you should carefully consider and

evaluate the risks and uncertainties described below. If any of these risks were to occur, our business, financial condition or results of operations would likely suffer. In that event, the value of our securities could decline, and you could lose part or all of your investment. The risks and uncertainties we describe are not the only ones facing us. Additional risks not presently known to us or that we currently deem immaterial may also impair our business, operations or prospects and could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

AxoGen's business involves a number of risks, some of which are beyond its control. The risk and uncertainties described below are not the only ones the Company faces. Set forth below is a discussion of the risks and uncertainties that management believes to be material to AxoGen.

Risks Related To Company

AxoGen has not experienced positive cash flow from its operations, and the ability to achieve positive cash flow from operations will depend on increasing sales of its products, which may not be achievable.

AxoGen has historically operated with negative cash flow from its operations. As of September 30, 2014, AxoGen had an accumulated deficit of approximately $83.6 million. If AxoGen product sales do not increase as anticipated, then it will continue to experience negative cash flows and adverse operating conditions. AxoGen's continuing capital needs and other factors could cause the Company to raise additional funds through public or private equity offerings, debt financings or from other sources. The sale of additional equity may result in dilution to AxoGen's shareholders. There is no assurance that AxoGen will be able to secure funding on terms acceptable to it, or at all.

AxoGen's revenue growth depends on its ability to expand its sales force, increase sales to existing customers and develop new customers, and there can be no assurance that these efforts will result in significant increase in sales.

AxoGen is in the process of investing in its sales channel composed of a combination of its direct sales force and independent distributors to allow it to increase sales to existing customers and reach new customers. There can be no assurance that these efforts will be successful in expanding AxoGen's product sales. AxoGen currently sells products directly through its employees and indirectly through distributor relationships. AxoGen is engaged in a major initiative to build and further expand sales and marketing capabilities. The incurrence of these expenses impacts AxoGen's operating results, and there can be no assurance of their effectiveness. If AxoGen is unable to develop its sales force, increase sales to existing customers and develop new customers, it may not be able to grow revenue or maintain its current level of revenue generation.

AxoGen's revenue depends primarily on three products.

Substantially all of AxoGen's revenue is currently derived from only three products, the Avance® Nerve Graft, AxoGuard® Nerve Protector and AxoGuard® Nerve Connector, for the treatment of peripheral nerve damage. Its ability to generate revenue is dependent on the success of these products. Accordingly, any disruption in AxoGen's ability to generate revenue from the sale of these products will have a material adverse impact on its business, results of operations, financial condition and growth prospects. In addition, AxoGen's expenditures for research and development are minimal and funding to develop, or increase efforts to find collaboration or licensing opportunities to obtain, additional products will be necessary.

The AxoGuard® products are only available through an exclusive distribution agreement with Cook Biotech. Our contract with Cook Biotech is for an initial seven year term and following such initial term, the agreement automatically renews for an additional seven (7) year period. AxoGen and Cook Biotech have agreed that the parameters for renewal have been met and the contract will automatically renew for the additional seven (7) year period. However, there are conditions for continuation of the agreement, including payment terms and minimum purchase requirements, that if breached could result in an earlier termination of the agreement; except that through mutual agreement the parties have not established such minimums and to date have not enforced such minimum purchase provision. Additionally, in the event that AxoGen and Cook Biotech were to fail to reach an agreement as to minimum purchase quantities, Cook Biotech could terminate the agreement if it was deemed that AxoGen had failed to generate commercially reasonable sales of AxoGuard® as measured by sales similar to a competitive product at the same stage in its commercial launch as verified by a mutually acceptable third-party. Although there are products that AxoGen believes it could develop or obtain that would replace the AxoGuard® products, the loss of the ability to sell the AxoGuard® products could have a material adverse effect on AxoGen's business until other replacement products are available.

Table of Contents

AxoGen's success will be dependent on continued acceptance of its products by the medical community.

Continued market acceptance of AxoGen's products will depend on its ability to demonstrate that its products are an attractive alternative to existing nerve reconstruction treatment options. Its ability to do so will depend on surgeons' evaluations of clinical safety, efficacy, ease of use, reliability, and cost-effectiveness of AxoGen's nerve repair products. For example, although AxoGen's Avance® Nerve Graft follows stringent safety standards, including sterilization by gamma irradiation, AxoGen believes that a small portion of the medical community has lingering concerns over the risk of disease transmission through the use of allografts in general. Furthermore, AxoGen believes that even if its products receive general acceptance within the medical community, acceptance and clinical recommendations by influential surgeons will be important to the commercial success of AxoGen's products.

Negative publicity concerning methods of donating human tissue and screening of donated tissue, in the industry in which AxoGen operates, may reduce demand for its Avance© Nerve Graft product and negatively impact the supply of available donor tissue.

AxoGen is highly dependent on its ability to recover cadaveric nerves from tissue donors for its Avance® Nerve Graft product. The availability of acceptable donors is relatively limited, and this availability is impacted by regulatory changes, general public opinion of the donation process and AxoGen's reputation for its handling of the donation process. Media reports or other negative publicity concerning both improper methods of tissue recovery from donors and disease transmission from donated cadaver tissue (allografts) including bones, tendon, etc. may limit widespread acceptance of AxoGen's Avance® Nerve Graft. Unfavorable reports of improper or illegal tissue recovery practices, both in the U.S. and internationally, as well as incidents of improperly processed tissue leading to transmission of disease, may broadly affect the rate of future tissue donation and market acceptance of allograft technologies. Potential patients may not be able to distinguish AxoGen products, technologies, and tissue recovery and processing procedures from others engaged in tissue recovery. In addition, unfavorable reports could make families of potential donors from whom AxoGen is required to obtain consent before processing tissue reluctant to agree to donate tissue to for-profit tissue processors. Any disruption in the supply could have negative consequences for AxoGen's revenue, operating results and continued operations.

AxoGen is highly dependent on the continued availability of its facilities and could be harmed if the facilities are unavailable for any prolonged period of time.

Any failure in the physical infrastructure of AxoGen's facilities, including the facility it leases from LifeNet Health, could lead to significant costs and disruptions that could reduce its revenues and harm its business reputation and financial results. Any natural or man-made event that impacts AxoGen's ability to utilize its facilities could have a significant impact on its operating results, reputation and ability to continue operations. This includes termination of the LifeNet Health facility lease which can occur upon six months' notice from either party. Although AxoGen believes it can find and make operational a new facility in less than six months, the regulatory process for approval of facilities is time-consuming and unpredictable. AxoGen's ability to rebuild or find acceptable lease facilities would take a considerable amount of time and expense and could cause a significant disruption in service to its customers. Although AxoGen has business interruption insurance which would, in instances other than lease termination, cover certain costs, it may not cover all costs nor help to regain AxoGen's standing in the market.

AxoGen must maintain high quality manufacturing and processing.

AxoGen's Avance® Nerve Graft is processed through its Avance® Process which requires careful calibration and precise, high-quality processing and manufacturing. Achieving precision and quality control requires skill and diligence by its personnel. If it fails to achieve and maintain these high quality controls, processing and manufacturing standards, including avoidance of manufacturing errors, defects or product failures, AxoGen could experience recalls or withdrawals of its product, delays in delivery, cost overruns or other problems that would adversely affect its business. AxoGen cannot completely eliminate the risk of errors, defects or failures. In addition, AxoGen may experience difficulties in scaling-up manufacturing of its Avance® product, including problems related to yields, quality control and assurance, tissue availability, adequacy of control policies and procedures, and lack of skilled personnel. If AxoGen is unable to process and produce its allografts on a timely basis, at acceptable quality and costs, and in sufficient quantities, or if it experiences unanticipated technological problems or delays in production, its business would be adversely affected.

AxoGen relies on third-party suppliers, some of which are currently the only source for the respective components or materials they supply to it.

Most of the raw materials used in the Avance® Process for the production of Avance® Nerve Graft are available from more than one supplier. However, one of the chemicals AxoGen uses in the manufacture of Avance® Nerve Graft is no longer provided by the original single source provider. AxoGen has inventory of such chemical which it believes provides more than one year of production. AxoGen is currently evaluating multiple avenues including a new supplier of the chemical and acceptable substitutes for the chemical. In addition, some of the test results, packaging and reagents/chemicals AxoGen uses in its manufacturing process are also obtained from single suppliers. We do not have written contracts with any of our single source suppliers, and at any time they could stop supplying our orders. FDA approval of a new supplier may be required if these materials become unavailable from AxoGen's current

Table of Contents

suppliers. Although there may be other suppliers that have equivalent materials that would be available to AxoGen, FDA approval of any alternate suppliers if required could take several months or years to obtain, if able to be obtained at all. Any delay, interruption or cessation of production by AxoGen's third-party suppliers of important materials, or any delay in qualifying new materials, if necessary, would prevent or delay AxoGen's ability to manufacture products. In addition, an uncorrected impurity, a supplier's variation in a raw material or testing, either unknown to AxoGen or incompatible with its manufacturing process, or any other problem with AxoGen's materials, testing or components, would prevent or delay its ability to manufacture products. These delays may limit AxoGen's ability to meet demand for its products and delay its clinical trial, which would have a material adverse impact on its business, results of operations and financial condition.

AxoGen relies on third parties to perform many necessary services for the commercialization of Avance® Nerve Graft, including services related to the recovery, distribution, storage and transportation.

AxoGen relies upon third parties for certain recovery, distribution, storage and transportation services. In accordance with product specifications, these third parties ship Avance® Nerve Graft in specially validated shipping containers at frozen temperatures. If any of the third parties that AxoGen relies upon in its recovery, distribution, storage or transportation process fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to AxoGen, or encounter physical damage or natural disaster at their facilities, AxoGen's ability to deliver product to meet commercial demand may be significantly impaired.

AxoGen is dependent on its relationships with distributors to generate revenue.

AxoGen derives material revenues through its relationships with distributors. If such distributor relationships were terminated for any reason, it could materially and adversely affect AxoGen's ability to generate revenues and profits. AxoGen intends to obtain the assistance of additional distributors to continue its sales growth. It may not be able to find additional distributors who will agree to market and distribute its products on commercially reasonable terms, if at all. If it is unable to establish new distribution relationships or renew current distribution agreements on commercially acceptable terms, operating results could suffer.

Loss of key members of management, who it needs to succeed, could adversely affect its business.

AxoGen's future success depends on the continued efforts of the members of its senior management team. Competition for experienced management personnel in the healthcare industry is intense. If one or more of AxoGen's senior executives or other key personnel are unable or unwilling to continue in their present positions, or if AxoGen is unable to attract and retain high quality senior executives or key personnel in the future, its business may be adversely affected.

AxoGen's operating results will be harmed if it is unable to effectively manage and sustain its future growth.

There can be no assurance that AxoGen will be able to manage its future growth efficiently or profitably. Its business is unproven on a large scale and actual revenue and operating margins, or revenue and margin growth, may be less than expected. If AxoGen is unable to scale its production capabilities efficiently, it may fail to achieve expected operating margins, which would have a material and adverse effect on its operating results. Growth may also stress AxoGen's ability to adequately manage its operations, quality of products, safety and regulatory compliance. If growth significantly decreases it will negatively impact AxoGen's cash reserves, and it may be required to obtain additional financing, which may increase indebtedness or result in dilution to shareholders. Further, there can be no assurance that AxoGen would be able to obtain additional financing on acceptable terms if all at.

There may be significant fluctuations in AxoGen's operating results.

Significant quarterly fluctuations in AxoGen's results of operations may be caused by, among other factors, its volume of revenues, seasonal changes in nerve repair activity, timing of sales force expansion and general economic conditions. There can be no assurance that the level of revenues and profits, if any, achieved by AxoGen in any particular fiscal period, will not be significantly lower than in other comparable fiscal periods. AxoGen's expense levels are based, in part, on its expectations as to future revenues. As a result, if future revenues are below expectations, net income or loss may be disproportionately affected by a reduction in revenues, as any corresponding reduction in expenses may not be proportionate to the reduction in revenues.

AxoGen's revenues depend upon prompt and adequate reimbursement from public and private insurers and national health systems.

Political, economic and regulatory influences are subjecting the healthcare industry in the U.S. to fundamental change. The ability of hospitals to pay fees for AxoGen's products depends in part on the extent to which reimbursement for the costs of such materials and related treatments will continue to be available from governmental health administration authorities, private health coverage insurers and other organizations. Major third-party payers of hospital services and hospital outpatient services, including Medicare, Medicaid and private healthcare insurers, annually revise their payment methodologies, which can result in stricter standards for reimbursement of hospital charges for certain medical procedures or the elimination of reimbursement. Further, Medicare, Medicaid and private healthcare insurer cutbacks could create downward price pressure on AxoGen's products.

Table of Contents

AxoGen may be subject to future product liability litigation that could be expensive and its insurance coverage may not be adequate.

Although AxoGen is not currently subject to any product liability proceedings, and it has no reserves for product liability disbursements, it may incur material liabilities relating to product liability claims in the future, including product liability claims arising out of the usage of AxoGen products. AxoGen currently carries product liability insurance in an amount consistent with industry averages, however, its insurance coverage and any reserves it may maintain in the future for product related liabilities may not be adequate and AxoGen's business could suffer material adverse consequences.

Technological change could reduce demand for AxoGen's products.

The medical technology industry is intensely competitive. AxoGen competes with both U.S. and international companies that engage in the development and production of medical technologies and processes including:

- biotechnology, orthopedic, pharmaceutical, biomaterial, chemical and other companies;
- academic and scientific institutions; and
- public and private research organizations.

AxoGen products compete with autograft, hollow-tube conduits and commercially available wraps, as well as with alternative medical procedures. For the foreseeable future, AxoGen believes a significant number of surgeons will continue to choose to perform autograft procedures when feasible, despite the necessity of performing a second operation and its drawbacks. In addition, many members of the medical community will continue to prefer the use of hollow-tube conduits due in part to their familiarity with these products and the procedures required for their use. Also, steady improvements have been made in synthetic human tissue substitutes, which could compete with AxoGen's products. Unlike allografts, synthetic tissue technologies are not dependent on the availability of human or animal tissue. Although AxoGen's growth strategy contemplates the introduction of new technologies, the development of these technologies is a complex and uncertain process, requiring a high level of innovation, as well as the ability to accurately predict future technology and market trends.

AxoGen may not be able to respond effectively to technological changes and emerging industry standards, or to successfully identify, develop or support new technologies or enhancements to existing products in a timely and cost effective manner, if at all. Finally, there can be no assurance that in the future AxoGen's competitors will not develop products that have superior performance or are less expensive relative to its products rendering them obsolete or noncompetitive. Due to its limited resources, its smaller size and its relatively early stage, AxoGen may face competitive challenges and barriers that are difficult to overcome and could negatively impact its growth

AxoGen may be unsuccessful in commercializing its products outside the U.S.

To date, AxoGen has focused its commercialization efforts in the U.S., except for minor revenues in the United Kingdom, Singapore, Switzerland, Spain, Austria, Israel and Canada. It intends to expand sales beyond these countries outside the U.S. and will need to comply with applicable foreign regulatory requirements, including obtaining the requisite approvals to do so. Additionally, AxoGen will need to either enter into distribution agreements with third parties or develop a direct sales force in these foreign markets. If it does not obtain adequate levels of reimbursement from third-party payers outside of the U.S., it may be unable to develop and grow its product sales internationally. Outside of the U.S., reimbursement systems vary significantly by country. Many foreign markets have government-managed healthcare systems that govern reimbursement for medical devices and procedures. Additionally, some foreign reimbursement systems provide for limited payments in a given period and therefore result in extended payment periods. If AxoGen is unable to successfully commercialize its products internationally, its long term growth prospects may be limited.

If AxoGen does not manage tissue and tissue donation in an effective and efficient manner, it could adversely affect its business.

Many factors affect the supply, quantity and timing of donor medical releases, such as effectiveness of donor screening (currently performed by donor recovery groups), the effective recovery of tissue, the timely receipt, recording and review of required medical documentation, and employee loss and turnover in AxoGen's and its contractor's recovery department. AxoGen can provide no assurance that tissue recovery or donor medical releases will occur at levels that will maximize processing efficiency and minimize AxoGen's cost per allograft processed.

Table of Contents

If AxoGen does not manage product inventory in an effective and efficient manner, it could adversely affect profitability.

Many factors affect the efficient use and planning of product inventory, such as effectiveness of predicting demand, effectiveness of preparing manufacturing to meet demand, efficiently meeting product mix and product demand requirements and product expiration. AxoGen may be unable to manage its inventory efficiently, keep inventory within expected budget goals, keep its work-in-process inventory on hand or manage it efficiently, control expired product or keep sufficient product on hand to meet demand, and AxoGen can provide no assurance that it can keep inventory costs within its target levels. Failing to do so may require AxoGen to raise additional cash resources or may harm long term growth prospects.

Our payment obligations under the Three Peaks Term Loan Agreement and Three Peaks Revenue Interest Agreement may adversely affect our financial position and our ability to obtain additional funds, and may increase our vulnerability to economic or business downturns.

We have borrowed $25 million under the Three Peaks Term Loan Agreement, and the indebtedness under the Three Peaks Term Loan Agreement is secured by substantially all of our tangible and intangible assets. We used the $25 million proceeds under the Three Peaks Term Loan Agreement, together with the $3.55 million proceeds from the registered direct offering to Three Peaks in November 2014 and $1.75 million cash from our own account, to pay off our obligations under the Revenue Interests Purchase Agreement by and between us and PDL BioPharma, Inc. dated October 5, 2012 (the "PDL Royalty Contract").

Outstanding debt could have important negative consequences to the holders of our securities, including the following:

- general domestic and global economic conditions;
- a portion of our cash flow from operations will be needed to pay debt service and will not be available to fund future operations;
- we have increased vulnerability to adverse general economic and industry conditions; and
- we may be vulnerable to higher interest rates because interest expense on our term loan is based on a variable rate.

In addition, we also entered into ten-year Revenue Interest Agreement (the "Three Peaks Revenue Interest Agreement") with Three Peaks. Royalty payments are based on a royalty rate of 3.75% of our revenues up to a maximum of $30 million in revenues in any 12 month period. In the event we make any subsequent borrowing under the Three Peaks Term Loan Agreement, the royalty rate increases proportionally up to a maximum of 4.80%. In addition, under the Three Peaks Revenue Interest Agreement, we are required to maintain certain covenants including those covenants under the Three Peaks Term Loan.

Payment requirements under the Three Peaks Term Loan Agreement and the Three Peaks Revenue Interest Agreement increase our cash burden. Our future operating performance is subject to market conditions and business factors that are beyond our control. If our cash flows and capital resources are insufficient to allow us to make required payments, we may have to reduce or delay capital expenditures, sell assets, seek additional capital or restructure or refinance our debt. If we raise funds by selling additional equity, such sale would result in dilution to our shareholders. There is no assurance that if we are required to secure funding we can do so on terms acceptable to us, or at all. Failure to pay interest or the principal amount when due would result in a default under the Three Peaks Term Loan Agreement and result in foreclosure on our assets which would have a material adverse effect.

The Three Peaks Term Loan Agreement and the Three Peaks Royalty Interest Agreement contain covenants that restrict our operations and failure to comply with the terms of such indebtedness could result in a default that could have material adverse consequences for us.

The Three Peaks Term Loan Agreement and the Three Peaks Royalty Interest Agreement contain covenants that place restrictions on our operations, including, without limitation, covenants related to debt restrictions, investment restrictions, dividend restrictions and restrictions on transactions with affiliates. Our ability to comply with these covenants may be affected by general economic and industry conditions, as well as market fluctuations and other events beyond our control. We do not know if we will be able to satisfy all such covenants in the future. Our breach of the covenants could result in a default under such agreement. In the event of a default under the Three Peaks Term Loan Agreement, the lender could require us to repay some of our outstanding debt prior to maturity, and/or to declare all amounts borrowed by us, together with accrued interest, to be due and payable. In the event that this occurs, we may be unable to repay all such accelerated indebtedness. Any indebtedness that we incur under the Three Peaks Term Loan Agreement is secured by substantially all of our tangible and intangible assets. If we default under the indebtedness secured by our assets, those assets would be available to the secured creditors to satisfy our obligations to the secured creditors.

AxoGen incurs costs as a result of operating as a public company, and its management is required to devote substantial time to compliance initiatives.

Table of Contents

As a public company, AxoGen incurs legal, accounting and other expenses to comply with relevant securities laws and regulations, including, without limitation, the requirement of establishment and maintenance of effective disclosure and financial controls and corporate governance practices. AxoGen's management devotes substantial time and financial resources to these compliance initiatives. Failure to comply with public company requirements could have a material adverse effect on AxoGen's business.

Our Business and Stock Price May Be Adversely Affected if Our Internal Controls Are Not Effective.

Section 404 of the Sarbanes-Oxley Act of 2002 requires companies to conduct a comprehensive evaluation of their internal control over financial reporting. To comply with this statute, each year we are required to document and test our internal control over financial reporting and our management is required to assess and issue a report concerning our internal control over financial reporting.

In our annual report for the period ended December 31, 2011, we reported a material weakness in our internal control over financial reporting, which related to an instance in which the accounting for a contract was inappropriately treated as an expense as opposed to a prepaid asset. Although we believe we took appropriate actions to remediate the control deficiencies we identified and to strengthen our internal control over financial reporting, we cannot assure you that we will not discover other material weaknesses in the future or that no material weakness will result from any difficulties, errors, delays or disruptions while we implement and transition to new internal systems. The existence of one or more material weaknesses could result in errors in our financial statements, and substantial costs and resources may be required to rectify these or other internal control deficiencies. If we cannot produce reliable financial reports, investors could lose confidence in our reported financial information, the market price of our common stock could decline significantly, we may be unable to obtain additional financing to operate and expand our business, and our business and financial condition could be harmed.

Our business and financial performance could be adversely affected, directly or indirectly, by disasters, by terrorist activities or by international hostilities.

Neither the occurrence nor the potential impact of disasters, terrorist activities and international hostilities can be predicted. However, these occurrences could impact us directly as a result of damage to our facilities or by preventing us from conducting our business in the ordinary course, or indirectly as a result of their impact on our customers, suppliers or other counterparties. We could also suffer adverse consequences to the extent that disasters, terrorist activities or international hostilities affect the financial markets or the economy in general or in any particular region.

Our ability to mitigate the adverse consequences of such occurrences is in part dependent on the quality of our resiliency planning, and our ability, if any, to anticipate the nature of any such event that occurs. The adverse impact of disasters or terrorist activities or international hostilities also could be increased to the extent that there is a lack of preparedness on the part of national or regional emergency responders or on the part of other organizations and businesses that we deal with, particularly those that we depend upon but have no control over.

Risks Related to the Regulatory Environment in which AxoGen Operates

AxoGen's business is subject to continuing regulatory compliance by the FDA and other authorities which is costly and could result in negative effects on its business.

AxoGen is subject to extensive regulation by foreign and domestic government entities and healthcare professionals, such as physicians, hospitals and those to whom and through whom we may market our products. We are subject to scrutiny under various federal, state and territorial laws in the United States and other jurisdictions in which we conduct business. These include, for example, anti-kickback laws, physician self-referral laws, false claims laws, criminal health care fraud laws, and anti-bribery laws e.g. the United States Foreign Corrupt Practices Act. Violations of these laws are punishable by criminal and/or civil sanctions, including, in some instances, fines, imprisonment and, within the United States, exclusion from participation in government healthcare programs, including Medicare, Medicaid and Veterans Administration health programs. These laws are administered by, among others, the U.S. Department of Justice, the Office of Inspector General of the Department of Health and Human Services, state attorneys general, and their respective counterparts in the applicable foreign jurisdictions in which we conduct business. Many of these agencies have increased their enforcement activities with

respect to medical device manufacturers in recent years.

Our products are also subject to regulation by the FDA. The FDA regulates the development, clinical testing, marketing, distribution, manufacturing, labeling, and promotion of biological products, such as that of AxoGen's Avance® Nerve Graft product. The FDA also regulates medical devices, for example, the AxoGuard® products. The FDA requires the approval of a biological product, like the Avance® Nerve Graft product, through a biological license application, or BLA, prior to marketing. Although the Avance® Nerve Graft product has not yet been approved by FDA through a BLA, FDA is permitting the product to be distributed, subject to FDA enforcement discretion, provided that AxoGen: (1) transitions to compliance with section 501(a)(2)(B) of the FD&C Act, the current good manufacturing practice regulations in 21 CFR Parts 210 and 211 and the applicable regulations and standards in

Table of Contents

21 CFR Parts 600-610 prior to initiation of a phase 3 clinical trial designed to demonstrate the safety, purity, and potency of the Avance® Nerve Graft; (2) conducts a phase 3 clinical trial to demonstrate safety, purity and potency of the Avance® Nerve Graft under an SPA; (3) continues to comply with the requirements of 21 CFR Part 1271; and (4) exercises due diligence in executing the transition plan.

The FDA also regulates medical devices and requires that certain medical devices, such as the AxoGuard® products, be cleared through the 510(k) premarket notification process prior to marketing. The FDA's premarket review process for new and modified existing devices that precedes product marketing can be time consuming and expensive. Some of the future products and enhancements to such products that AxoGen expects to develop and market may require marketing clearance or approval from the FDA. There can be no assurance, however, that clearance or approval will be granted with respect to any of AxoGen's device products or enhancements of marketed products or that AxoGen's Avance® Nerve Graft will achieve an effective IND or ultimately an approved BLA. FDA review of AxoGen's devices or biological products may encounter significant delays during FDA's premarket review process that would adversely affect AxoGen's ability to market its products or enhancements. In addition, there can be no assurance that AxoGen products, including the Avance® Nerve Graft, or enhancements will not be subject to a lengthy and expensive approval process with the FDA.

It is possible that if regulatory clearances or approvals to market a product are obtained from the FDA, the clearances or approvals may contain limitations on the indicated uses of such product and other uses may be prohibited. Product approvals by the FDA can also be withdrawn due to failure to comply with regulatory standards or the occurrence of unforeseen problems following initial approval. Also, the FDA could limit or prevent the distribution of AxoGen products and has the power to require the recall of such products. FDA regulations depend heavily on administrative interpretation, and there can be no assurance that future interpretations made by the FDA or other regulatory bodies will not adversely affect AxoGen's operations. AxoGen, and its facilities, may be inspected by the FDA from time to time to determine whether it is in compliance with various regulations relating to specifications, development, documentation, validation, testing, quality control, and product labeling. A determination that AxoGen is in violation of such regulations could lead to imposition of civil penalties, including fines, product recalls or product seizures and, in certain cases, criminal sanctions.

The use, misuse or off-label use of AxoGen's products may harm its reputation or the image of its products in the marketplace, or result in injuries that lead to product liability suits, which could be costly to AxoGen's business or result in FDA sanctions if the company is deemed to have engaged in off-label promotion. AxoGen is seeking a biologics license through the BLA process for specific uses of Avance® Nerve Graft under specific circumstances. Its promotional materials and training methods must comply with FDA requirements and other applicable laws and regulations, including the prohibition against off-label promotion. AxoGen's promotion of the AxoGuard® products, which are regulated as medical devices, also must comply with FDA's requirements and must only use labeling that is consistent with the specific indication(s) for use included in FDA's substantial equivalence order that results in marketing the devices. The FDA does not restrict or regulate a physician's use of a medical product within the practice of medicine, and AxoGen cannot prevent a physician from using its products for an off-label use. However, the Federal Food, Drug, and Cosmetic Act, referred to herein as the FD&C Act, and the FDA's regulations restrict the kind of promotional communications that may be made about AxoGen's products and if the FDA determines that AxoGen's promotional or training materials constitute the unlawful promotion of an off-label use, it could request that AxoGen modify its training or promotional materials and/or subject the Company to regulatory or enforcement actions, including the issuance of an untitled letter, a warning letter, civil money penalties, seizure, injunction or criminal fines and penalties. Other federal, state or foreign governmental authorities might also take action if they consider AxoGen promotion or training materials to constitute promotion of an uncleared or unapproved use, which could result in significant fines or penalties under other statutory authorities, such as laws prohibiting false claims for reimbursement, or exclusion from participation in federal health programs. In that event, AxoGen's reputation could be damaged and the use of its products in the marketplace could be impaired.

In addition, there may be increased risk of injury if physicians or others attempt to use AxoGen products off-label. Furthermore, the use of AxoGen's product for indications other than those for which its products have been approved, cleared or licensed by the FDA may not effectively treat the conditions not referenced in product indications, which could harm AxoGen's reputation in the marketplace among physicians and patients. Physicians may also misuse AxoGen's product or use improper techniques if they are not adequately trained in the particular use, potentially leading to injury and an increased risk of product liability. Product liability claims are expensive to defend and could divert management's attention from its primary business and result in substantial damage awards against AxoGen. Any of these events could harm AxoGen's business, results of operations and financial condition.

AxoGen's Avance® Nerve Graft product is currently allowed to be distributed pursuant to a transition plan with the FDA and a change in position by the FDA regarding its use of enforcement discretion to permit the sale of Avance would have a material adverse effect on AxoGen.

The FDA considers the AxoGen's Avance® Nerve Graft product to be a biological product, subject to BLA approval requirements. Although the Avance® Nerve Graft product has not yet been approved by FDA through a BLA, AxoGen's Avance® Nerve Graft product is currently distributed under the controls applicable to a HCT/P pursuant to section 361 of the Public Health

Table of Contents

Service Act and 21 CFR Part 1271 of FDA's regulations, subject to FDA's enforcement discretion and AxoGen's compliance with a transition plan established by the FDA. AxoGen has continued to communicate with FDA's CBER since the acceptance of the transition plan on clinical trial design, preclinical studies, Chemistry, Manufacturing, and Controls ("CMC") for the Avance® Nerve Graft., and other issues related to the pending IND Subject to the FDA's enforcement discretion, AxoGen can commercially distribute the Avance® Nerve Graft until FDA makes a final determination on an Avance® Nerve Graft BLA submission, assuming AxoGen remains in compliance with the transition plan and exercises due diligence in executing the transition plan. In the event that the FDA becomes dissatisfied with AxoGen's progress or actions with respect to the transition plan or FDA changes its position for any reason regarding its use of enforcement discretion to permit AxoGen to distribute and sell the Avance® Nerve Graft product in accordance with the transition plan, AxoGen would no longer be able to sell the Avance® Nerve Graft product, which would have a material adverse effect on AxoGen's operations and financial viability. In addition, if AxoGen does not meet the conditions of the transition plan, or fails to comply with applicable regulatory requirements, the FDA could impose civil penalties, including fines, product seizures, injunctions or product recalls and, in certain cases, criminal sanctions. These consequences also would have a material adverse effect on AxoGen's operations and financial viability.

AxoGen's AxoGuard® products are subject to FDA and other regulatory requirements.

AxoGen's AxoGuard® product line is regulated as a medical device under the FD&C Act and subject to premarket notification and clearance requirements under section 510(k) of the FD&C Act, 21 CFR Part 820 (Quality System Regulation) and other FDA regulations. AxoGen distributes for Cook Biotech Incorporated the AxoGuard® product line and Cook Biotech is responsible for the regulatory compliance of the AxoGuard® product line. Cook Biotech has obtained a 510(k) premarket clearance from the FDA for porcine (pig) small intestine submucosa for the repair of peripheral nerve discontinuities where gap closure can be achieved by flexion of the extremity. Cook Biotech has also obtained a 510(k) premarket clearance for the AxoGuard® Nerve Protector for the repair of peripheral nerve injuries in which there is no gap or where a gap closure is achieved by flexion of the extremity. If AxoGen or Cook Biotech Incorporated fails to comply with applicable regulatory requirements, the FDA could deny or withdraw 510(k) clearance for the AxoGuard® products, or impose civil penalties, including fines, product seizures or product recalls and, in certain cases, criminal sanctions.

Defective AxoGen product could lead to recall or other negative business conditions.

If AxoGen's products are defective or otherwise pose safety risks, the FDA could require their recall, or AxoGen may initiate a voluntary recall of its products. The FDA may require recall of a marketed medical device product, such as the AxoGuard® products, in the event that it determines that the medical device presents a reasonable probability of serious adverse health consequences or death. However, most device recalls do not rise to this level of health significance, and result from voluntary action. FDA has authority to recall biological products when a batch, lot or other quantity of the product presents an imminent or substantial hazard to the public health. However, the agency usually requests voluntary recalls of biological products, such as the Avance® Nerve Graft. If a company does not comply with an FDA request for a recall, FDA can order one under the above-referenced circumstances or take other enforcement actions, such as product seizure. In addition, manufacturers may, on their own initiative, recall a product to remove or correct a deficiency or to remedy a violation of the FD&C Act of an unacceptable risk to health, reports of safety issues, failures, manufacturing errors, design or labeling defects or other deficiencies and issues. Recalls and other field corrections for any of AxoGen's products would divert managerial and financial resources and have an adverse effect on its business, results of operations and financial condition. A recall could harm AxoGen's reputation with customers and negatively affect its sales. AxoGen may initiate recalls involving some of its products in the future that it determines do not require notification of the FDA. If the FDA were to disagree with AxoGen's determinations, it could request that it report those actions as recalls, and take regulatory or enforcement action against AxoGen or the product.

If AxoGen's products cause or contribute to a death, a serious injury or any adverse reaction involving a communicable disease related to its products, or malfunction in certain ways, it will be subject to reporting regulations, which can result in voluntary corrective actions or agency enforcement actions. If AxoGen fails to report these events to the FDA within the required timeframes, or at all, the FDA could take regulatory or enforcement action against AxoGen. Any adverse event involving AxoGen's products could result in future voluntary corrective actions, such as recalls or customer notifications, or agency action, such as inspection, mandatory recall or other enforcement action. Any corrective action, whether voluntary or involuntary, as well as AxoGen defending itself in a lawsuit, would require the dedication of time and capital, distract management from operating its business, and may harm AxoGen's reputation, business, results of operations and financial condition.

AxoGen's manufacturing operations must comply with FDA and other governmental requirements.

AxoGen's manufacturing operations require it to comply with the FDA's and other governmental authorities' laws and regulations regarding the manufacture and production of medical products, which is costly and could subject AxoGen to enforcement action. Any of these actions could impair AxoGen's ability to produce its products in a cost-effective and timely manner in order to meet customer demands. AxoGen may also be required to bear other costs or take other actions that may have an adverse impact on its future sales and its ability to generate profits. Furthermore, AxoGen key material suppliers, licensors and or other contractors may not

Table of Contents

continue to be in compliance with all applicable regulatory requirements, which could result in AxoGen's failure to produce its products on a timely basis and in the required quantities, if at all.

Sales of AxoGen human tissue products outside the U.S. are subject to foreign regulatory requirements that vary from country to country. In the E.U., human tissue regulations, if applicable, differ from one E.U. member state to the next. Because of the absence of a harmonized regulatory framework and the proposed regulation for advanced therapy medicinal products in the E.U., as well as for other countries, the approval process for human derived cell or tissue based medical products may be extensive, lengthy, expensive and unpredictable. AxoGen products will be subject to E.U. member states' regulations that govern the donation, procurement, testing, coding, traceability, processing, preservation, storage, and distribution of human tissues and cells and cellular or tissue-based products. In addition, some E.U. member states have their own tissue banking regulations. The inability to meet foreign regulatory requirements could materially affect AxoGen's future growth and compliance with such requirements could place a significant financial burden on AxoGen.

Clinical trials can be long, expensive and ultimately uncertain which could jeopardize AxoGen's ability to obtain regulatory approval and continue to market its Avance® Nerve Graft product.

AxoGen is required to perform a clinical trial for its Avance® Nerve Graft pursuant to requirements of the FDA to obtain approval of a BLA for the product. This trial is expensive, is expected to take several years to execute, and is subject to factors within and outside of AxoGen's control. The outcome of this trial is uncertain.

AxoGen submitted an IND for the Avance® Nerve Graft in April, 2013. On June 7, 2013, the FDA placed the IND on Clinical Hold, pending the FDA's receipt of additional information relating to the potency, mechanical characterization, and labeling of the product. The phase 3 clinical trial cannot begin until the FDA lifts the Clinical Hold. AxoGen is developing the data and information to respond to the FDA's requests, but there can be no assurance that an effective IND will be obtained on a timely basis or at all. Additionally AxoGen was audited by the FDA in March 2013 and the quality system was found to be in compliance with 21 CFR Part 1271. AxoGen is working to ensure compliance with the applicable regulations by having ongoing discussions on the transition of the quality system to 21 CFR Parts 210/211 and 600-610 regulations with the FDA and being audited by the FDA for compliance to 21 CFR Part1271 of the regulations. Final determination of regulatory compliance will be made during FDA's pre-license inspection as part of the BLA review. If FDA is unable to agree with AxoGen, or AxoGen is unable to meet the standards required of it by the FDA, regarding preclinical studies, clinical studies and CMC, the approval of AxoGen's BLA would become impossible or delayed.

AxoGen continues to work diligently with the FDA and, in this context, continues to distribute the Avance® Nerve Graft products. The FDA will end the period of enforcement discretion upon a final determination of AxoGen's BLA submission or if the FDA finds that AxoGen does not meet the conditions for the transition plan, or is not exercising due diligence in executing the transition (e.g., not progressing toward the IND submission, study completion, or BLA submission in a timely or adequate fashion). If final action on the BLA is negative or AxoGen is found to not meet the conditions for the transition plan or its execution, AxoGen will not be able to continue to distribute the Avance® Nerve Graft, and AxoGen's business and financial condition will be materially adversely affected.

The results of non-clinical studies do not necessarily predict future clinical trial results, and predecessor clinical trial results may not be repeated in subsequent clinical trials. Additionally, the FDA may disagree with AxoGen's interpretation of the data from its non-clinical studies and clinical trials and may require the company to pursue additional non-clinical studies or clinical trials, or not approve AxoGen's BLA. If AxoGen is unable to demonstrate the safety and efficacy of its product through its clinical trials, it will be unable to obtain regulatory approval to market the Avance® Nerve Graft and will not be able to continue to sell it.

AxoGen will rely on third parties to conduct its clinical trial and they may not perform as contractually required or expected.

AxoGen will rely on third parties, such as contract research organizations ("CROs"), medical institutions, clinical investigators and contract laboratories to conduct its clinical trial and certain non-clinical studies. AxoGen and its CROs are required to comply with all applicable regulations governing clinical research, including good clinical practice, or GCP. The FDA enforces these regulations through periodic inspections of trial sponsors, principal investigators, CROs and trial sites. If AxoGen or its CROs fail to comply with applicable FDA regulations, the data generated in its clinical trials may be deemed unreliable and the FDA may require AxoGen to perform additional clinical trials before approving its applications. AxoGen cannot be certain that, upon inspection, the FDA and similar foreign regulatory authorities will determine that AxoGen's clinical trial complies or complied with clinical trial regulations, including GCP. In addition, AxoGen's clinical trial must be conducted with product produced under applicable current Good Manufacturing Practice, or GMP, regulations. Failure to comply with the clinical trial regulations may require AxoGen to repeat clinical trials, which would delay the regulatory approval process. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, if these third parties need to be replaced, or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to AxoGen's clinical protocols or regulatory requirements or for other

Table of Contents

reasons, AxoGen's non-clinical development activities or clinical trials may be extended, delayed, suspended or terminated, and it would not be able to obtain regulatory approval for, its products on a timely basis, if at all, and its business, results of operations, financial condition and growth prospects would be adversely affected. Furthermore, AxoGen's third-party clinical trial investigators may be delayed in conducting its clinical trials for reasons outside of their control.

U.S. governmental regulation could restrict the use of AxoGen's Avance® Nerve Graft product, restrict AxoGen's procurement of tissue or increase costs.

In addition to the FDA requirements for biological products, the Avance® Nerve Graft will continue to be subject to various requirements for human tissue under 21 CFR Part 1271 controls. Human tissues intended for transplantation have been regulated by the FDA since 1993. In May 2005, three new comprehensive regulations went into effect that address manufacturing activities associated with

HCT/P. The first requires that companies that produce and distribute HCT/Ps register with the FDA. The second provides criteria that must be met for donors to be eligible to donate tissues and is referred to as the "Donor Eligibility" rule. The third rule governs the processing and distribution of the tissues and is often referred to as the Current Good Tissue Practices rule. The Current Good Tissue Practices rule covers all stages of allograft processing, from procurement of tissue to distribution of final allografts. Together, they are designed to ensure that sound, high quality practices are followed to reduce the risk of tissue contamination and of communicable disease transmission to recipients. These regulations increased regulatory scrutiny within the industry in which AxoGen operates and have led to increased enforcement actions, which affects the conduct of its business. See "Business — Government Regulations." These regulations can also increase the cost of tissue recovery activities. Additionally, the Avance® Nerve Graft is subject to certain state and local regulations, as well as compliance to the standards of the tissue bank industry's accrediting organization, the American Association of Tissue Banks ("AATB").

The procurement and transplantation of allograft nerve tissue is also subject to federal law pursuant to the National Organ Transplant Act ("NOTA"), a criminal statute which prohibits the purchase and sale of human organs used in human transplantation, including nerve and related tissue, for "valuable consideration." NOTA only permits reasonable payments associated with the removal, transportation, processing, preservation, quality control, implantation and storage of human nerve tissue. AxoGen makes payments to certain of its clients and tissue banks for their services related to recovering allograft nerve tissue on its behalf. If NOTA is interpreted or enforced in a manner which prevents AxoGen from receiving payment for services it renders, or which prevents it from paying tissue banks or certain of its clients for the services they render for AxoGen, its business could be materially and adversely affected.

AxoGen has engaged, through its marketing employees, independent sales agents and sales representatives, in ongoing efforts designed to educate the medical community as to the benefits of AxoGen products, and AxoGen intends to continue its educational activities. Although AxoGen believes that NOTA permits payments in connection with these educational efforts as reasonable payments associated with the processing, transportation and implantation of AxoGen products, payments in connection with such education efforts are not exempt from NOTA's restrictions and AxoGen's inability to make such payments in connection with its education efforts may prevent it from paying AxoGen sales representatives for their education efforts and could adversely affect AxoGen's business and prospects. No federal agency or court has determined whether NOTA is, or will be, applicable to every allograft nerve tissue-based material which AxoGen's processing technologies may generate. Assuming that NOTA applies to AxoGen's processing of allograft nerve tissue, AxoGen believes that it complies with NOTA, but there can be no assurance that more restrictive interpretations of, or amendments to, NOTA will not be adopted in the future, which would call into question one or more aspects of AxoGen's method of operations.

Other regulatory entities include state agencies with statutes covering tissue banking. Regulations issued by Florida, New York, California and Maryland, among others, will be particularly relevant to AxoGen's business. Most states do not currently have tissue banking regulations. However, incidents of allograft related infections in the industry may stimulate the development of regulation in other states. It is possible that others may make allegations against AxoGen or against donor recovery groups or tissue banks about non-compliance with applicable FDA regulations or other relevant statutes or regulations. Allegations like these could cause regulators or other authorities to take investigative or other action, or could cause negative publicity for AxoGen's business and the industry in which it operates.

Healthcare policy changes may have a material adverse effect on AxoGen.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, which substantially changes the way healthcare is financed by both governmental and private insurers, and encourages improvements in the quality of healthcare items and services. This Act significantly impacts the biotechnology and medical device industries and could have a material adverse impact on numerous aspects of AxoGen's business.

This Act includes, among other things, the following measures:

Table of Contents

- a 2.3% excise tax on any entity that manufactures or imports medical devices offered for sale in the U.S., with limited exceptions, beginning in 2013, referred to as the Device Tax;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities and conduct comparative clinical effectiveness research;
- new reporting and disclosure requirements on healthcare manufacturers for any "transfer of value" made or distributed to physicians and teaching hospitals, as well as reporting of certain physician ownership interests ("Sunshine Act");
- payment system reforms including a national pilot program on payment bundling to encourage hospitals, physicians and other providers to improve the coordination, quality and efficiency of certain healthcare services through bundled payment models;
- an independent payment advisory board that will submit recommendations to reduce Medicare spending if projected Medicare spending exceeds a specified growth rate; and
- a new abbreviated pathway for the licensure of biologic products that are demonstrated to be biosimilar or interchangeable with a licensed biologic product.

Because the Avance® Nerve Graft is a biological product and is not a medical device it is not subject to the Device Tax. Cook Biotech is the manufacturer of the AxoGuard® products and AxoGen is the distributor. As such, Cook Biotech is responsible for payment of the Device Tax on the transfer price of the AxoGuard® products from Cook Biotech to AxoGen and AxoGen has no further Device Tax obligations with respect to its resale. There can be no assurance that changes in regulations will not subject it to such obligations in the future.

There are also a number of states (such as Vermont, Massachusetts, Minnesota) with their own Sunshine Acts that implement the reporting and disclosure requirements on healthcare manufacturers for any "transfer of value" made or distributed to physicians and teaching

hospitals, as well as reporting of certain physician ownership interests.

In the future, there may continue to be additional proposals relating to the reform of the U.S. healthcare system. Certain of these proposals could limit the prices AxoGen is able to charge for its products or the amounts of reimbursement available for its products and could also limit the acceptance and availability of its products. The adoption of some or all of these proposals could have a material adverse effect on AxoGen's business, results of operations and financial condition.

Additionally, initiatives sponsored by government agencies, legislative bodies and the private sector to limit the growth of healthcare costs, including price regulation and competitive pricing, are ongoing in markets where AxoGen does business. AxoGen could experience an adverse impact on operating results due to increased pricing pressure in the U.S. and in other markets. Governments, hospitals and other third-party payors could reduce the amount of approved reimbursement for AxoGen's products or deny coverage altogether. Reductions in reimbursement levels or coverage or other cost-containment measures could unfavorably affect AxoGen's future operating results.

Risks Related to AxoGen's Intellectual Property

Failure to protect AxoGen's Intellectual Property rights could result in costly and time consuming litigation and its loss of any potential competitive advantage.

AxoGen's success will depend, to a large extent, on its ability to successfully obtain and maintain patents, prevent misappropriation or infringement of intellectual property, or IP, maintain trade secret protection, and conduct operations without violating or infringing on the IP rights of third parties. See "Business — Intellectual Property." There can be no assurance that AxoGen's patented and patent pending technologies will provide it with a competitive advantage, that AxoGen will be able to develop or acquire additional technology that is patentable, or that third parties will not develop and offer technologies which are similar to AxoGen's. Moreover, AxoGen can provide no assurance that confidentiality agreements with its employees, consultants and other parties, trade secrecy agreements or similar agreements intended to protect unpatented technology will provide the intended protection. IP litigation is extremely expensive and time-consuming, and it is often difficult, if not impossible, to predict the outcome of such litigation. A failure by AxoGen to protect its IP could have a materially adverse effect on its business and operating results and its ability to successfully compete in its industry.

Future protection for AxoGen's proprietary rights is uncertain which may impact its ability to successfully compete in its industry.

The degree of future protection for AxoGen's proprietary rights is uncertain. AxoGen cannot ensure that:

- it, or its licensors, were the first to make the inventions covered by each of AxoGen's patents;
- it, or its licensors, were the first to file patent applications for these inventions;

Table of Contents

- others will not independently develop similar or alternative technologies or duplicate any of AxoGen's technologies;
- any of AxoGen's pending patent applications will result in issued patents;
- any of AxoGen's issued patents or those of its licensors will be valid and enforceable;
- any patents issued to AxoGen or its collaborators will provide any competitive advantages or will not be challenged by third parties;
- it will develop additional proprietary technologies that are patentable;
- the patents of others will not have a material adverse effect on its business rights; or
- the measures AxoGen relies on to protect its IP underlying their products may not be adequate to prevent third parties from using its technology, all of which could harm its ability to compete in the market.

AxoGen's commercial success depends in part on its ability and the ability of its collaborators and licensors to avoid infringing patents and proprietary rights of third parties which could expose it to litigation or commercially unfavorable licensing arrangements. Third parties may accuse AxoGen or collaborators and licensors of employing their proprietary technology in AxoGen products, or in the materials or processes used to research or develop AxoGen products, without authorization. Any legal action against AxoGen collaborators, licensors or it claiming damages and/or seeking to stop AxoGen's commercial activities relating to the affected products, materials and processes could, in addition to subjecting AxoGen to potential liability for damages, require it or its collaborators and licensors to obtain a license to continue to utilize the affected materials or processes or to manufacture or market the affected products. AxoGen cannot predict whether AxoGen or its collaborators and licensors would prevail in any of these actions or whether any license required under any of these patents would be made available on commercially reasonable terms, if at all. If AxoGen were unable to obtain such a license, it and its collaborators and licensors may be unable to continue to utilize the affected materials or processes, or manufacture or market the affected products, or AxoGen may be obligated by a court to pay substantial royalties and/or other damages to the patent holder. Even if AxoGen were able to obtain such a license, the terms of such a license could substantially reduce the commercial value of the affected product or products and impair AxoGen's prospects for profitability. Accordingly, AxoGen cannot predict whether, or to what extent, the commercial value of the affected product or products, or AxoGen's prospects for profitability may be harmed as a result of any of the liabilities discussed above. Furthermore, infringement and other IP claims, with or without merit, can be expensive and time-consuming to litigate and can divert management's attention from its core business. AxoGen and its licensors may be unable to obtain and enforce IP rights to adequately protect its products and related IP.

The patent protection for our products may expire before we are able to maximize their commercial value which may subject us to increased competition and reduce or eliminate our opportunity to generate product revenue.

The patents for our commercialized products and products in development have varying expiration dates and, when these patents expire, we may be subject to increased competition and we may not be able to recover our development costs. For example, U.S. patents covering the formulations used in our AxoGuard® product line, which are held by Cook Biotech, are scheduled to expire from August 17 2017 through November 2018. Although we expect that Cook Biotech is using best efforts to take any action possible to extend the life of these patents, there can be no assurance that any action is possible or action taken will be successful. If these patents expire while we have the right to distribute and market the AxoGuard® products, it could adversely affect our ability to successfully execute our business strategy to maximize the value of AxoGuard® products and could likely negatively impact our future financial condition and results of operations.

Others may claim an ownership interest in AxoGen IP which could expose it to litigation and have a significant adverse effect on its prospects.

A third party may claim an ownership interest in one or more of AxoGen's patents or other IP. A third party could bring legal actions against AxoGen claiming it infringes their patents or proprietary rights, and seek monetary damages and/or enjoin clinical testing, manufacturing and marketing of the affected product or products. While AxoGen believes it owns the right, title and interest in the patents for which it or its licensors have applied and AxoGen's other IP (including that which is licensed from third parties), and is presently unaware of any claims or assertions by third-parties with respect to AxoGen's patents or IP, it cannot guarantee that a third-party will not assert a claim or an interest in any of such patents or IP. If AxoGen becomes involved in any litigation, it could consume a substantial portion of AxoGen's resources, and cause a significant diversion of effort by AxoGen's technical and management personnel regardless of the outcome of the litigation. If any of these actions were successful, in addition to any potential liability for damages, AxoGen could be required to obtain a license to continue to manufacture or market the affected product, in which case AxoGen may be required to pay substantial royalties or grant cross-licenses to AxoGen's patents. AxoGen cannot, however, assure you that any such license will be available on acceptable terms, if at all. Ultimately, AxoGen could be prevented from commercializing a product, or be forced to cease some aspect of its business operations as a result of claims of patent infringement or violation of other IP rights, which could have a material and adverse effect on AxoGen's business, financial condition, and results of operations. Further, the outcome of IP litigation is subject to uncertainties that cannot be adequately quantified in advance, including the demeanor and credibility of witnesses and the identity of the adverse party. This is especially true in IP cases that may turn on the testimony of experts as to technical facts upon which experts may reasonably disagree.

Table of Contents

AxoGen depends on maintenance of exclusive licenses.

AxoGen depends fundamentally on keeping and satisfying the terms of exclusive licenses of its nerve repair technologies from UFRF and UT where the original technologies are purported to be invented. Though AxoGen makes an effort to follow these agreements strictly, a disagreement between AxoGen and either party could have negative impacts on its ability to operate its business effectively. In addition, AxoGen could learn that the technologies it has licensed from UFRF and UT do not perform as purported, are not efficacious, or are not the property of UFRF or UT, or some similar problem with the license, any of which would have an immediate and negative impact on AxoGen's business.

Risk Related to Our Common Stock

The price of AxoGen's common shares could be highly volatile due to a number of factors, which could lead to losses by investors and costly securities litigation.

Our common shares are listed on the NASDAQ Capital Market under the symbol "AXGN." The trading price of our common shares has experienced substantial volatility and is likely to continue to be highly volatile in response to a number of factors including, without limitation, the following:

- limited daily trading volume resulting in the lack of a liquid market;
- fluctuations in price and volume due to investor speculation and other factors that may not be tied to the financial performance of AxoGen;
- performance by AxoGen in the execution of its business plan;
- financial viability; actual or anticipated variations in our operating results;
- announcements of developments by us or our competitors;
- market conditions in our industry;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- adoption of new accounting standards affecting our industry;
- additions or departures of key personnel;
- introduction of new products by us or our competitors;
- sales of our common shares or other securities in the open market;
- regulatory developments in both the United States and foreign countries;
- performance of products sold and advertised by licensees in the marketplace;
- economic and other external factors;
- period-to-period fluctuations in financial results; and
- other events or factors, many of which are beyond our control.

The stock market is subject to significant price and volume fluctuations. In the past, and several recent situations, following periods of

volatility in the market price of a company's securities, securities class action litigation has been initiated against such company. Litigation initiated against us, whether or not successful, could result in substantial costs and diversion of our management's attention and resources, which could harm our business and financial condition.

We do not anticipate paying any cash dividends in the foreseeable future.

The continued operation and expansion of our business will require substantial funding. In addition, the Three Peaks Term Loan places certain restrictions on our ability to pay dividends. Accordingly, we do not anticipate that we will pay any cash dividends on our common shares for the foreseeable future. Any determination to pay dividends in the future will be at the discretion of our board of directors and will depend upon results of operations, financial condition, contractual restrictions, restrictions imposed by applicable law and other factors our board of directors deems relevant. Accordingly, if you purchase shares, realization of a gain on your investment will depend on the appreciation of the price of our common shares, which may never occur. Investors seeking cash dividends in the foreseeable future should not purchase our common shares.

Anti-takeover provisions in Minnesota law may deter acquisition bids for us that you might consider favorable.

We are governed by the provisions of Sections 302A.671, 302A.673 and 302A.675 of the Minnesota Business Corporation Act (the "MBCA"). These provisions may discourage a negotiated acquisition or unsolicited takeover of us and deprive our shareholders of an opportunity to sell their shares at a premium over the market price.

Table of Contents

In general, Section 302A.671 of the MBCA provides that a corporation's shares acquired in a control share acquisition have no voting rights unless voting rights are approved in a prescribed manner. A "control share acquisition" is a direct or indirect acquisition of beneficial ownership of shares that would, when added to all other shares beneficially owned by the acquiring person, entitle the acquiring person to have voting power of 20% or more in the election of directors.

In general, Section 302A.673 of the MBCA prohibits a public Minnesota corporation from engaging in a business combination with an interested shareholder for a period of four years after the date of the transaction in which the person became an interested shareholder, unless the business combination is approved in a prescribed manner. The term "business combination" includes mergers, asset sales and other transactions resulting in a financial benefit to the interested shareholder. An "interested shareholder" is a person who is the beneficial owner, directly or indirectly, of 10% or more of a corporation's voting stock, or who is an affiliate or associate of the corporation, and who, at any time within four years before the date in question, was the beneficial owner, directly or indirectly, of 10% or more of the corporation's voting stock. Section 302A.673 does not apply if a committee of our Board of Directors consisting of all of its disinterested directors (excluding current and former officers) approves the proposed transaction or the interested shareholder's acquisition of shares before the interested shareholder becomes an interested shareholder.

If a tender offer is made for our common shares, Section 302A.675 of the MBCA precludes the offeror from acquiring additional shares of stock (including in acquisitions pursuant to mergers, consolidations or statutory share exchanges) within two years following the completion of the tender offer, unless shareholders selling their shares in the later acquisition are given the opportunity to sell their shares on terms that are substantially the same as those contained in the earlier tender offer. Section 302A.675 does not apply if a committee of our Board of Directors consisting of all of its disinterested directors (excluding its current and former officers) approves the proposed acquisition before any shares are acquired pursuant to the earlier tender offer.

Risks Related to this Offering

As a new investor, you will incur substantial dilution as a result of this offering and future equity issuances, and as a result, our share price could decline.

The offering price will be substantially higher than the net tangible book value per share of our outstanding common shares. As a result, based on the net tangible book value of our common shares as of September 30, 2014, an investor purchasing common shares in this offering will incur immediate and substantial dilution of $ per share, based on the sale of shares of our common stock at the public offering price of $ per share, and after deducting the underwriting discount and estimated offering expenses payable by us. See the section entitled "Dilution" on page S-25 of this prospectus supplement for a more detailed discussion of the dilution you will incur if you purchase common shares in this offering.

In addition, pursuant to the equity purchase provisions in the Three Peaks Term Loan Agreement, in the event that we sell our securities at a lower price per share than the $2.58 per share public offering price paid by Three Peaks in our registered direct offering of common shares to Three Peaks in November 2014, or where the terms of such subsequent sale are otherwise more favorable, then in such case we have agreed to match the more favorable terms of such subsequent sale with respect to the shares purchased by Three Peaks. A subsequent sale does not include the issuance of securities or options to our employees, officers, directors or consultants pursuant to our approved employee option pool or any other employee stock purchase or option plan existing as of November 12, 2014.

Subject to market conditions and other factors, we may pursue raising additional funds in the future, as we continue to build our business. In future years, we will likely need to raise additional funding to finance our operations and to fund clinical trials, regulatory submissions and the development, manufacture and marketing of other products under development and new product opportunities. Accordingly, we may conduct future offerings of equity or debt securities. The exercise of outstanding options and warrants and future equity issuances, including future public offerings or future private placements of equity securities and any additional shares issued in connection with acquisitions, will also result in dilution to investors. In addition, the market price of our common shares could fall as a result

of resales of any of these common shares.

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

We may in the future issue additional shares of our common stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any other offering or other transactions at a price per share that is equal to or greater than the price per share paid by investors in this offering. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering.

Table of Contents

In addition, we have a substantial number of stock options outstanding. To the extent that outstanding stock options have been or may be exercised or other shares issued, investors purchasing our common stock in this offering may experience further dilution.

We will have broad discretion in how we use the proceeds from this offering, and our use of the offering proceeds may not yield a favorable return on your investment.

We currently anticipate that the net proceeds from this offering will be used primarily for continued expansion of our sales force and surgeon education and general working capital purposes. Pending the application of the net proceeds, we intend to invest the net proceeds in investment-grade, interest-bearing securities. Our management has broad discretion over how these proceeds are used and could spend the proceeds in ways with which you may not agree, and the proceeds may not be invested in a manner that yields a favorable or any return. Our failure to use these funds effectively could have a material adverse effect on our business.

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds of this offering, after deducting the underwriting discount and estimated offering expenses payable by us, will be approximately $ million ($ million if the underwriter exercises the overallotment option in full).

We intend to use the net proceeds of this offering for continued expansion of our sales force and surgeon education and general corporate purposes. Our management will retain broad discretion over the allocation of the net proceeds from the sale of the common shares. We have no current understandings, agreements or commitments for any material acquisitions.

Therefore, the investor will be relying on the judgment of our management, who will have broad discretion regarding the application of the proceeds of this offering. The amounts and timing of our actual expenditures will depend upon numerous factors, including the amount of cash generated by our operations, our cash needs, the rate of adoption of our products by the medical community and efficiency of our product development. We may find it necessary or advisable to use portions of the proceeds from this offering for other purposes.

Pending the application of the net proceeds, we intend to invest the net proceeds in investment-grade, interest-bearing securities. Our management has broad discretion over how these proceeds are used and could spend the proceeds in ways with which you may not agree, and the proceeds may not be invested in a manner that yields a favorable or any return.

DIVIDEND POLICY

We currently intend to retain earnings, if any, to finance the growth and development of our business, and do not expect to pay any cash dividends to its shareholders in the foreseeable future. In additional, the Three Peaks Term Loan Agreement places certain restrictions on our ability to pay dividends.

Table of Contents

CAPITALIZATION

The following table describes our capitalization as of September 30, 2014:

- on an actual basis; and
- on an as adjusted basis to give effect to the sale of of our shares in this offering at the public offering price of $ per share, after deducting estimated offering expenses;

You should read this capitalization table together with our consolidated financial statements and the related notes and other financial information incorporated by reference in this prospectus supplement and the accompanying prospectus and the "Use of Proceeds" section.

	As of September 30, 2014	
	Actual	As Adjusted
	(in thousands, except share and per share data)	
Long-term debt (1)	$ 28,174	$ 28,174
Shareholders' equity (deficit):		
Common Share, $.01 par value; 50,000,000 shares authorized, 17,466,381 shares issued and outstanding (2)	175	
Additional paid-in capital (3)	73,264	
Accumulated deficit	(83,625)	(83,625)
Total shareholders' equity (deficit)	(10,186)	
Total capitalization	$ 17,988	$

(1) On November 12, 2014, we entered into the Three Peaks Term Loan Agreement, under which we borrowed $25 million. We used the $25 million proceeds under the Three Peaks Term Loan Agreement, together with the $3.55 million proceeds from the registered direct offering to Three Peaks in November 2014 and $1.75 million cash from our own account, to pay off our obligations under the PDL Royalty Contract. As a result, our obligations to PDL under the PDL Royalty Contract were extinguished.

(2) AxoGen had 19,488,814 shares outstanding on February 2, 2015, excluding: 2,889,310 common shares issuable upon the exercise of options outstanding as of February 2, 2015 at a weighted average exercise price of $3.06 per share; and 89,686 common shares issuable upon the exercise of warrants outstanding as of February 2, 2015 at an exercise price of $2.23 per share.

(3) Represents additional paid-in capital, net of estimated issuance costs of $.

Information in the above table is based on 17,466,381 shares outstanding on September 30, 2014, assumes no exercise by the underwriter of its over-allotment option to purchase up to an additional shares to cover over-allotments, if any, and excludes:

- 2,298,033 common shares issuable upon the exercise of options outstanding as of September 30, 2014 at a weighted average exercise price of $2.94 per share;
- 89,686 common shares issuable upon the exercise of warrants outstanding as of September 30, 2014 at an exercise price of $2.23 per share; and
- 911,548 additional common shares reserved for future issuance as of September 30, 2014 under our 2010 Stock Incentive Plan.

Table of Contents

DILUTION

The purchaser of common shares offered by this prospectus supplement and the accompanying prospectus will suffer immediate and substantial dilution in the net tangible book value per share of common share. Our net tangible book value as of September 30, 2014 was approximately $(10.8) million, or $(0.62) per common share. Net tangible book value per share is determined by dividing our total tangible assets less total liabilities by the actual number of outstanding shares of our common shares. After giving effect to our issuance of shares at the public offering price of $ per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our net tangible book value as of September 30, 2014 would have been $ million or $ per common share. This represents an immediate increase in pro forma net tangible book value of $ per share to our existing shareholders and an immediate dilution of $ per share to new investors in this offering. The following table illustrates this per share dilution:

Public offering price per share		$
Net tangible book value per share as of September 30, 2014	$ (0.62)	
Increase per share attributable to this offering	$	
Pro forma net tangible book value per share after this offering		$
Dilution per share to new investor		$

Information in the above table is based on 17,466,381 shares outstanding on September 30, 2014, assumes no exercise by the underwriter of its over-allotment option to purchase up to an additional shares to cover over-allotments, if any, and excludes:

- 2,298,033 common shares issuable upon the exercise of options outstanding as of September 30, 2014, at a weighted average exercise price of $2.94 per share;
- 89,686 common shares issuable upon the exercise of warrants outstanding as of September 30, 2014, at an exercise price of $2.23 per share; and
- 911,548 additional common shares reserved for future issuance as of September 30, 2014, under our 2010 Stock Incentive Plan.

If the underwriter exercises in full its option to purchase additional common shares at the public offering price of $ per share, the as adjusted net tangible book value deficit after this offering would be $ per share, representing an increase in net tangible book value of $ per share to existing shareholders and immediate dilution in net tangible book value of $ per share to purchasers

in this offering at the public offering price.

Dilution per share to new investors is determined by subtracting pro forma net tangible book value per share after this offering from the public offering price per share paid by a new investor. Pro forma calculation here reflects only an adjustment to September 30, 2014 information related specifically to the proceeds from, and shares issued, in this offering. It does not reflect any other changes to our financial or equity position of including, but not limited to, the Three Peaks Term Loan Agreement, issuance of an additional 2,022,433 common shares, issuance of an additional stock options to purchase 605,000 common shares or in cash and cash equivalents.

If any shares are issued in connection with outstanding options or warrants, you will experience further dilution. Pursuant to the equity purchase provisions in the Three Peaks Term Loan Agreement, in the event that we sell our securities at a lower price per share than the $2.58 per share public offering price paid by Three Peaks in our registered direct offering of common shares to Three Peaks in November 2014, or where the terms of such subsequent sale are otherwise more favorable, then in such case we have agreed to match the more favorable terms of such subsequent sale with respect to the shares purchased by Three Peaks. A subsequent sale does not include the issuance of securities or options to our employees, officers, directors or consultants pursuant to our approved employee option pool or any other employee stock purchase or option plan existing as of November 12, 2014.

Table of Contents

UNDERWRITING

We have entered into an underwriting agreement with Wedbush Securities Inc., as underwriter, with respect to the shares being offered by this prospectus supplement. Subject to certain conditions, we have agreed to sell to the underwriter, and the underwriter has agreed to purchase from us, shares at the public offering price, less a discount of % of the public offering price.

The underwriting agreement provides that the obligation of the underwriter to purchase the shares offered hereby is subject to certain conditions and that the underwriter is obligated to purchase all of the shares offered hereby if any are purchased.

The underwriter proposes to offer to the public the shares purchased pursuant to the underwriting agreement at the public offering price on the cover page of this prospectus supplement. It is expected that delivery of the shares of common stock offered hereby will be made through the facilities of the Depository Trust Company.

Commissions and Discounts

The following table shows the per share and total underwriting discount to be paid to the underwriter by us at the public offering price listed on the cover page of this prospectus, less underwriting discount. Such amounts are shown assuming both no exercise and full exercise of the underwriter's option to purchase additional shares.

	Per Share	Total without Over-Allotment Option	Total with Over-Allotment Option
Public Offering Price	$	$	$
Underwriting Discount	$	$	$
Proceeds, before expenses, to us	$	$	$

We estimate that the total expenses payable by us, but excluding the underwriting discount, will be approximately $. We have agreed to reimburse the underwriter for certain out-of-pocket expenses up to a maximum of $150,000. In no event will the total compensation payable to the underwriter and any other member of the Financial Industry Regulatory Authority, Inc., or FINRA, or independent broker-dealer (including any financial advisor) in connection with the sale of the common stock offered hereby exceed 8.0% of the gross proceeds of this offering.

Option to Purchase Additional Shares

We have granted an option to the underwriter, exercisable for 30 days after the date of this prospectus supplement, to purchase up to additional shares at the public offering price, less the underwriting discount, solely to cover over-allotments, if any.

Lock-Up Agreements

We, our directors and executive officers and De Novo Ventures have entered into lock-up agreements with the underwriter prior to the commencement of this offering pursuant to which we and each of these persons, with limited exceptions, for a period of 90 days after the date of this prospectus supplement, may not, without the prior written consent of the underwriter, (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, or file (or participate in the filing of) a registration statement with the SEC in respect of, any of our common shares or any securities convertible into or exercisable or exchangeable for our common shares (including without limitation, our common shares which may be deemed to be beneficially owned by the undersigned in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant), (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the shares, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of our common shares or such other securities, in cash or otherwise, (3) make any demand for, or exercise any right with respect to, the registration of any of our common shares or any security convertible into or exercisable or exchangeable for our common shares, or (4) publicly announce an intention to effect any transaction specified in clause (1), (2) or (3) above.

Notwithstanding the foregoing, if (1) during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to our company occurs; or (2) prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day period, then in each case the restrictions imposed by the lock-up agreement shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event, unless the underwriter waives, in writing,

Table of Contents

such extension. The underwriter has agreed to waive such extension if the provisions of FINRA Rule 2711(f)(4) are not applicable to this offering.

In addition, in connection with our registered direct offering of common shares to PDL in November 2014, PDL has agreed that the 643,382 shares it purchased in the registered direct offering will be subject to a lock-up until November 12, 2015, under which PDL will not transfer, sell, convey, contract to sell (including pursuant to any derivative instrument) or otherwise dispose, in each case, for consideration the shares without the written consent of our board of directors. We have agreed with the underwriter that we will not waive the PDL lock-up before the expiration or termination of the lock-up agreements our directors and officers have entered into in connection with this offering.

Indemnification

We have agreed to indemnify the underwriter against certain liabilities, including liabilities under the Securities Act.

Stabilization, Short Positions and Penalty Bids

The underwriter may engage in stabilizing transactions, short sales and purchases to cover positions created by short sales, and penalty bids or purchases for the purpose of pegging, fixing or maintaining the price of our common shares, in accordance with Regulation M under the Exchange Act:

- Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum.

- A short position involves a sale by the underwriter of shares in excess of the number of shares the underwriter is obligated to purchase in the offering, which creates the syndicate short position. This short position may be either a covered short position or a naked short position. In a covered short position, the number of shares involved in the sales made by the underwriter in excess of the number of shares it is obligated to purchase is not greater than the number of shares that it may purchase by exercising their option to purchase additional shares. In a naked short position, the number of shares involved is greater than the number of shares in its option to purchase additional shares. The underwriter may close out any short position by either exercising their option to purchase additional shares and/or purchasing shares in the open market. In determining the source of shares to close out the short position, the underwriter will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through its option to purchase additional shares. A naked short position is more likely to be created if the underwriter is concerned that there could be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.

- Syndicate covering transactions involve purchases of the common stock in the open market after the distribution has been completed in order to cover syndicate short positions.

- Penalty bids permit the representative to reclaim a selling concession from a syndicate member when the common shares originally sold by the syndicate member is purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common shares or preventing or retarding a decline in the market price of our common shares. As a result, the price of our common shares may be higher than the price that might otherwise exist in the open market. These transactions may be effected on the NASDAQ Capital Market or otherwise and, if commenced, may be discontinued at any time.

Neither we nor the underwriter make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor the underwriter make any representation that the underwriter will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Listing on The NASDAQ Capital Market

Our common shares are traded on The NASDAQ Capital Market under the symbol “AXGN.”

Table of Contents

Electronic Distribution

In connection with the offering, the underwriter or securities dealers may distribute this prospectus supplement and the accompanying prospectus by electronic means, such as e-mail.

Other Relationships

The underwriter may provide from time to time in the future certain financial advisory, investment banking and other services to us and our affiliates in the ordinary course of their business, for which they may receive customary fees and commissions. In addition, from time to time, the underwriter and its affiliates may effect transactions for their own account or the accounts of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

Table of Contents

NOTICE TO INVESTORS

Notice to Investors in the United Kingdom

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State") an offer to the public of any securities which are the subject of the offering contemplated by this prospectus supplement and the related prospectus may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any such securities may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(a) to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;

(b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;

(c) by the underwriter to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive); or

(d) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of these securities shall result in a requirement for the publication by the issuer or the underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any of the securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any such securities to be offered so as to enable an investor to decide to purchase any such securities, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

The underwriter has represented, warranted and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated any invitation or inducement to engage in investment activity (within the meaning of section 21 of the Financial Services and Markets Act 2000 (the FSMA)) received by it in connection with the issue or sale of any of the securities in circumstances in which section 21(1) of the FSMA does not apply to the issuer; and

(b) it has complied with and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom.

European Economic Area

In particular, this document does not constitute an approved prospectus in accordance with European Commission's Regulation on Prospectuses no. 809/2004 and no such prospectus is to be prepared and approved in connection with this offering. Accordingly, in relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (being the Directive of the European Parliament and of the Council 2003/71/EC and including any relevant implementing measure in each Relevant Member State) (each, a Relevant Member State), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the Relevant Implementation Date) an offer of securities to the public may not be made in that Relevant Member State prior to the publication of a prospectus in relation to such securities which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of securities to the public in that Relevant Member State at any time:

- to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;

- to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000; and (3) an annual net turnover of more than €50,000,000, as shown in the last annual or consolidated accounts; or

- in any other circumstances which do not require the publication by the Issuer of a prospectus pursuant to Article 3 of the Prospectus Directive.

Table of Contents

For the purposes of this provision, the expression an "offer of securities to the public" in relation to any of the securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State. For these purposes the shares offered hereby are "securities."

Table of Contents

LEGAL MATTERS

Certain legal matters in connection with the securities offered hereby will be passed upon for us by Morgan, Lewis & Bockius LLP, Philadelphia, Pennsylvania and Kaplan, Strangis and Kaplan, P.A., Minneapolis, Minnesota. Certain legal matters in connection with this offering will be passed upon for the underwriter by Lowenstein Sandler LLP, New York, New York.

EXPERTS

The consolidated financial statements of AxoGen, Inc. and subsidiary as of December 31, 2013 and 2012, and for each of the years then ended have been incorporated by reference in this prospectus supplement in reliance upon the report of Lurie Besikof Lapidus & Company, LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus are only parts of a registration statement on Form S-3 (File No. 333-195588) that we filed with the SEC under the Securities Act and do not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document.

We are a public company and file proxy statements, annual, quarterly and special reports and other information with the SEC. The registration statement, such reports and other information can be inspected and copied at the Public Reference Room of the SEC located at 100 F Street, N.E., Washington D.C. 20549. Copies of such materials, including copies of all or any portion of the registration statement, can be obtained from the Public Reference Room of the SEC at prescribed rates. You can call the SEC at 1-800-SEC-0330 to obtain information on the operation of the Public Reference Room. Such materials may also be accessed electronically by means of the SEC's home page on the Internet (www.sec.gov).

We make our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports available through our website, free of charge, as soon as reasonably practicable after we file such material with, or furnish it to the SEC. Our website address is www.axogeninc.com. We have included our website address in this prospectus supplement solely as an inactive textual reference. The information contained on, or that can be accessed through, our website is not part of this prospectus supplement.

Table of Contents

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with the SEC, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to

be part of this prospectus supplement and the accompanying prospectus. Information contained in this prospectus supplement and the accompanying prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus supplement and the accompanying prospectus will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings (other than Current Reports on Form 8-K furnished under Item 2.02 or Item 7.01 and exhibits filed on such form that are related to such items) we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the prospectus supplement and until the termination of this offering:

- our Annual Report on Form 10-K for the year ended December 31, 2013;
- our Quarterly Reports on Form 10-Qs for the fiscal quarters ended March 31, 2014, June 30, 2014 and September 30, 2014;
- our Current Reports on Form 8-K filed with the SEC on January 8, 2014, May 12, 2014, May 18, 2014, August 25, 2014, November 13, 2014 (as amended by Amendment No. 1 on Form 8-K/A filed with the SEC on February 4, 2015), December 31, 2014 and February 4, 2015;
- our Definitive Proxy Statement on Schedule 14A filed with the SEC on March 31, 2014; and
- the description of our common shares set forth in our registration statement on Form 8-A filed with the SEC on August 6, 2013, including any amendments or reports filed for the purpose of updating such description.

To receive a free copy of any of the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, other than any exhibits, unless the exhibits are specifically incorporated by reference into this prospectus, call or write us at the following address and telephone number:

AxoGen, Inc.
13631 Progress Boulevard, Suite 400
Alachua, Florida 32615
(386) 462-680

Table of Contents

PROSPECTUS

$35,000,000

Common Stock

This prospectus relates to offers and resales of up to $35,000,000 of our common shares. We will bear all costs, expenses and fees in connection with the registration of these securities.

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

Our common shares trade on the NASDAQ Capital Market under the symbol “AXGN.” On April 29, 2014, the last reported sale price of our common shares on the NASDAQ Capital Market was $2.56 per share.

As of April 29, 2014, the aggregate market value of our outstanding common stock held by non-affiliates, or public float, was approximately $27,487,823 based on 17,466,091 shares of outstanding common stock, of which approximately 6,728,660 shares were held by affiliates, and a price of $2.56 per share, which was the last reported sale price of our common stock on The NASDAQ Capital Market on April 29, 2014. We have not offered any securities pursuant to General Instruction I.B.6 of Form S-3 during the prior 12 calendar month period that ends on and includes the date of this prospectus. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities registered on this registration statement in a public primary offering with a value exceeding more than one-third of our public float in any 12-month period so long as our public float remains below $75.0 million.

Investing in our securities involves a high degree of risk. You should carefully review and consider the risks and uncertainties described under the heading “Risk Factors” on page 3 of this prospectus and in any applicable prospectus supplement, any free writing prospectus or any documents incorporated by reference.

This prospectus may not be used to offer or sell any securities unless accompanied by a prospectus supplement.

The securities described in this prospectus may be sold directly by us to investors, through agents designated from time to time or to

or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus and in the applicable prospectus supplement. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that we expect to receive from such sale will also be set forth in a prospectus supplement.

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

This prospectus is dated May 9, 2014.

Table of Contents

TABLE OF CONTENTS

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, utilizing a "shelf" registration process. Under this shelf registration process, we may offer our common shares in one or more offerings, up to a total dollar amount of $35,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer common shares under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of the offering. We may also add, update or change in the prospectus supplement any of the information contained in this prospectus or in the documents that we have incorporated by reference into this prospectus. We urge you to carefully read this prospectus and any applicable prospectus supplement, together with the information incorporated by reference herein as described under the headings "Where You Can Find More Information" and "Information Incorporated by Reference" before buying any of the securities being offered. **THIS PROSPECTUS MAY NOT BE USED TO OFFER OR SELL SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.**

You should rely only on the information that we have provided or incorporated by reference in this prospectus, any applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you. We have not authorized anyone to provide you with different information. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we may authorize to be provided to you. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading "Where You Can Find Additional Information." In this prospectus, unless the context specifically indicates otherwise, the terms "the Company," "AxoGen," "we," "us" and "our" refer to AxoGen, Inc. and its subsidiaries.

Table of Contents

ABOUT AXOGEN, INC.

We are a leading medical technology company dedicated to advancing the science and commercialization of peripheral nerve repair solutions. Peripheral nerves provide the pathways for both motor and sensory signals throughout the body and their damage can result in the loss of muscle function and/or feeling.

Nerves can be damaged in a number of ways. When a nerve is cut due to a traumatic injury or surgery, functionality of the nerve may be compromised, causing the nerve to no longer carry the signals to and from the brain to the muscles and skin. This type of injury generally requires a surgical repair. The traditional gold standard has been to either suture the nerve ends together directly without tension or to bridge the gap between the nerve ends with a less important nerve surgically removed from elsewhere in the patient's own body referred to as nerve autograft. In addition, pressure on a nerve or blunt force trauma can cause nerve injuries that may require surgical intervention.

In order to improve the options available for the surgical repair and regeneration of peripheral nerves, AxoGen has developed and licensed patented and patent pending regenerative medicine technologies. AxoGen's innovative approach to regenerative medicine has resulted in first-in-class products that it believes are redefining the peripheral nerve repair market. AxoGen's products offer a full suite of surgical nerve repair solutions including Avance® Nerve Graft, the only off-the-shelf commercially available processed nerve allograft, human nerve tissue obtained from a donor, for bridging severed nerves without the comorbidities of a nerve autograft second surgical site, such as loss of feeling where the nerve was removed and potential pain at the donor site. The Company's AxoGuard® line of products is a natural scaffold ExtraCellular Matrix, or ECM, derived from pig tissue. AxoGuard® Nerve Connector is used as a coaptation aid to facilitate the tensionless repair of severed nerves, and AxoGuard® Nerve Protector is used to wrap and protect injured peripheral nerves and reinforce the nerve reconstruction while preventing soft tissue attachments.

AxoGen's products are used by surgeons during surgical interventions to repair a wide variety of nerve injuries throughout the body. These injuries range from a simple laceration of a finger to a complex brachial plexus injury (an injury to the network of nerves that originate in the neck) as well as nerve injuries caused by dental and other surgical procedures. Avance® Nerve Graft provides surgeons bridging material with the micro-architecture of a human nerve. This structure is essential and allows for bridging nerve gaps or discontinuities up to 70mm in length. Additionally, Avance® Nerve Graft has product and sales synergies with AxoGuard® Nerve Protector and AxoGuard® Nerve Connector. AxoGuard® products provide the unique features of pliability, suturability, and translucence for visualization of the underlying nerve, while also allowing the patient's own cells to incorporate into the extracellular matrix to remodel and form a tissue similar to the outermost layer of the nerve (nerve epineurium).

We have reported a net loss of approximately $14,557,000 and $9,418,000 for the years ended December 31, 2013 and 2012, respectively, and a net loss of approximately $4,240,000 and $3,434,000 for the three months ended March 31, 2014 and 2013, respectively.

We were incorporated under the laws of Minnesota in 1977. Our principal executive offices are located at 13631 Progress Boulevard, Suite 400, Alachua, Florida 32615 and our telephone number is (386) 462-6800. Our website address is www.axogeninc.com. We have included our website address in this prospectus solely as an inactive textual reference. The information contained on, or that can be accessed through, our website is not part of this prospectus.

Table of Contents

RISK FACTORS

Investing in our securities involves a high degree of risk. Before purchasing our securities, you should carefully consider the risks and uncertainties described under "Risk Factors" in Item 1A of our most recent Annual Report on Form 10-K for the year ended December 31, 2013 and filed with the SEC on March 6, 2014, as well as information incorporated by reference into this prospectus, any applicable prospectus supplement or any free writing prospectus. If any of these risks were to occur, our business, financial condition or results of operations would likely suffer. In that event, the value of our securities could decline, and you could lose part or all of your investment. The risks and uncertainties we describe are not the only ones facing us. Additional risks not presently known to us or that we currently deem immaterial may also impair our business operations.

Table of Contents

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain statements contained or incorporated by reference into this prospectus, any applicable prospectus supplement and any free writing prospectus, constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Securities Exchange Act. These forward-looking statements may concern possible or anticipated future results of operations or business developments. These statements are based on management's current expectations or predictions of future conditions, events or results based on various assumptions and management's estimates of trends and economic factors in the markets in which we are active, as well as our business plans. Words such as "expects", "anticipates", "intends", "plans", "believes", "seeks", "estimates", "projects", "forecasts", "may", "should", variations of such words and similar expressions are intended to identify such forward-looking statements. The forward-looking statements may include, without limitation, statements regarding product development, product potential, regulatory environment, sales and marketing strategies, capital resources or operating performance. The forward-looking statements are subject to risks and uncertainties, which may cause results to differ materially from those set forth in the statements. Forward-looking statements should be evaluated together with the many uncertainties that

affect the Company's business and its market, particularly those discussed in the risk factors and cautionary statements in the Company's filings with the Securities and Exchange Commission, including as described in "Risk Factors" contained or incorporated by reference in this prospectus and in any related free writing prospectus and any applicable prospectus supplement, and in our most recent Annual Report on Form 10-K, as well as any amendments thereto reflected in subsequent filings with the SEC.

Forward-looking statements are not guarantees of future performance, and actual results may differ materially from those projected. The forward-looking statements are representative only as of the date they are made, and the Company assumes no responsibility to update any forward-looking statements except as required by law.

Table of Contents

USE OF PROCEEDS

Except as described in any prospectus supplement or in any related free writing prospectus that we may authorize to be provided to you, we currently intend to use the net proceeds from the sale of the securities offered hereby for continued product commercialization and marketing efforts, development of product pipeline, including product line extension, and for general corporate purposes , including working capital, acquisitions, capital expenditures and repayment of indebtedness.

Our management will retain broad discretion over the allocation of the net proceeds from the sale of the securities. We have no current understandings, agreements or commitments for any material acquisitions.

Table of Contents

PLAN OF DISTRIBUTION

We may sell the securities, from time to time, to or through underwriters, dealers or agents, or directly to one or more purchasers pursuant to:

- underwritten public offerings;
- negotiated transactions;
- block trades;
- "at the market offerings," within the meaning of Rule 415(a)(4) of the Securities Act, to or through a market maker or into an existing trading market, on an exchange or otherwise, at prevailing market prices; or
- through a combination of these methods.

We may distribute securities from time to time in one or more transactions:

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

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

- the name or names of the underwriters, if any;
- if the securities are to be offered through the selling efforts of brokers or dealers, the plan of distribution and the terms of any agreement, arrangement, or understanding entered into with broker(s) or dealer(s) prior to the effective date of the registration statement, and, if known, the identity of any broker(s) or dealer(s) who will participate in the offering and the amount to be offered through each;
- the purchase price of the securities and the proceeds we will receive from the sale;
- if any of the securities being registered are to be offered otherwise than for cash, the general purposes of the distribution, the basis upon which the securities are to be offered, the amount of compensation and other expenses of distribution, and by whom they are to be borne;
- any delayed delivery arrangements;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- any public offering price;
- any discounts, commissions or commissions allowed or reallowed or paid to dealers;
- the identity and relationships of any finders, if applicable; and
- any securities exchange or market on which the securities may be listed.

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

If underwriters are used in the sale, the obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by

managing underwriters or by underwriters without a syndicate. Unless otherwise indicated in the prospectus supplement, subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. The securities will be acquired by the underwriters for their own accounts and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Any initial public offering price and any discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time.

The securities may be sold to a dealer as principal. The dealer may resell the securities to the public at varying prices to be determined by the dealer at the time of resale. Any such dealer may be deemed to be an underwriter of the securities offered and sold.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the prospectus

Table of Contents

supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may sell securities directly to one or more purchasers without using underwriters or agents. Underwriters, dealers and agents that participate in the distribution of the securities may be underwriters as defined in the Securities Act, and any discounts or commissions they receive from us and any profit on their resale of the securities may be treated as underwriting discounts and commissions under the Securities Act.

If indicated in the applicable prospectus supplement, we may authorize underwriters or their other agents to solicit offers by certain institutional investors to purchase securities from us pursuant to contracts providing for payment and delivery at a future date. Institutional investors with which these contracts may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and others. In all cases, these purchasers must be approved by us. The obligations of any purchaser under any of these contracts will not be subject to any conditions except that (a) the purchase of the securities must not at the time of delivery be prohibited under the laws of any jurisdiction to which that purchaser is subject and (b) if the securities are also being sold to underwriters, the issuer(s) must have sold to these underwriters the securities not subject to delayed delivery. Underwriters and other agents will not have any responsibility in respect of the validity or performance of these contracts.

Agents, underwriters, dealers and remarketing firms may be entitled under relevant agreements entered into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act or to contribution with respect to payments which the agents, underwriters or dealers may be required to make.

Our common shares are listed on the NASDAQ Capital Market under the symbol “AXGN.”

In connection with an offering, the underwriters may purchase and sell the offered securities in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of offered securities than they are required to purchase in an offering. Stabilizing transactions consist of certain bids or purchases made for the purpose of preventing or retarding a decline in the market price of the offered securities while an offering is in progress.

The underwriters also may impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the underwriters have repurchased offered securities sold by or for the account of that underwriter in stabilizing or short-covering transactions.

These activities by the underwriters may stabilize, maintain or otherwise affect the market price of the offered securities. As a result, the price of the offered securities may be higher than the price that otherwise might exist in the open market. If these activities are commenced, they may be discontinued by the underwriters at any time.

Underwriters, dealers and agents, or their affiliates, may be customers of, engage in transactions with, or perform services for, us and our subsidiaries in the ordinary course of business.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered by this prospectus will be passed upon for us by Kaplan, Strangis and Kaplan, P.A., Minneapolis, Minnesota.

EXPERTS

The consolidated financial statements of AxoGen, Inc. and subsidiary as of December 31, 2013 and 2012, and for each of the years then ended have been incorporated by reference in this registration statement in reliance upon the report of Lurie Besikof Lapidus & Company, LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement that we filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. We are a public company and file proxy statements, annual, quarterly and special reports and other information with the SEC. The registration statement, such reports and other information can be inspected and copied at the Public Reference Room of the SEC located at 100 F Street, N.E., Washington D.C. 20549. Copies of such materials, including copies of all or any portion of the registration statement, can be obtained from the Public Reference Room of the SEC at prescribed rates. You can call the SEC at 1-800-SEC-0330 to obtain information on the operation of the Public Reference Room. Such materials may also be accessed electronically by means of the SEC's home page on the Internet (www.sec.gov).

You should rely only on the information provided in this prospectus. We have not authorized anyone to provide you with different information. You should not assume that the information in this document is accurate as of any date other than that on the front cover of this prospectus.

Table of Contents

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring to those documents. The information incorporated by reference is an important part of this prospectus. Any statement contained in a document which is incorporated by reference in this prospectus is automatically updated and superseded if information contained in this prospectus, or information that we later file with the SEC, modifies or replaces this information. We incorporate by reference the documents listed below and any future documents we subsequently file pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act (other than information furnished to, and not filed with, the SEC) prior to the termination of this offering:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2013;
- our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2014; and
- our Current Report on Form 8-K filed with the SEC on January 8, 2014;
- the description of our common stock our registration statement on Form 8-A filed with the SEC on August 6, 2013, including any amendments or reports filed for the purpose of updating such description.

To receive a free copy of any of the documents incorporated by reference in this prospectus, other than any exhibits, unless the exhibits are specifically incorporated by reference into this prospectus, *call* or *write* us at the following address and telephone number:

AxoGen, Inc.
13631 Progress Boulevard, Suite 400
Alachua, Florida 32615
(386) 462-6800

Table of Contents

Shares

AXOGEN, INC.

Common Shares

PROSPECTUS SUPPLEMENT

February , 2015