Use these links to rapidly review the document
Table of Contents
TABLE OF CONTENTS

Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-224713

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered[1]	Proposed Maximum Offering Price Per Unit	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee[2]
Common stock, $0.01 par value per share	3,450,000	$41.00	$141,450,000	17,610.53

(1) Includes 450,000 shares of common stock that may be purchased by the underwriters upon exercise of their option to purchase additional shares of common stock.

(2) Calculated in accordance with Rule 456(b) and Rule 457(r) under the Securities Act of 1933, as amended.

Table of Contents

PROSPECTUS SUPPLEMENT
(To Prospectus dated May 7, 2018)

3,000,000 Shares

AxoGen, Inc.

Common Stock

We are offering 3,000,000 shares of our common stock. Our common stock is traded on the Nasdaq Capital Market ("Nasdaq") under the symbol "AXGN." On May 8, 2018, the last sale price of our common stock, as reported on Nasdaq, was $43.35 per share.

Investing in our securities involves a high degree of risk. These risks are described under the caption "Risk Factors" beginning on page S-5 of this prospectus supplement.

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

	Per Share	Total
Public offering price	$ 41.00	$ 123,000,000
Underwriting discounts and commissions[(1)]	$ 2.46	$ 7,380,000
Proceeds, before expenses, to us	$ 38.54	$ 115,620,000

(1) See "Underwriting" for a complete description of the compensation payable to the underwriters.

We have granted the underwriters an option to purchase up to an aggregate of 450,000 additional shares at the public offering price, less the underwriting discounts and commissions, for a period of 30 days following the date of this prospectus supplement. If the underwriters exercise in full their option, the total underwriting discounts and commissions payable by us will be $8,487,000, and the total proceeds to us, before expenses, will be $132,963,000.

The underwriters expect to deliver the shares to the purchasers against payment on or about May 11, 2018 through the book-entry facilities of The Depository Trust Company.

Joint Book-Running Managers

Jefferies **Leerink Partners**

Co-Managers

William Blair **JMP Securities**

Prospectus Supplement dated May 8, 2018

Table of Contents
Prospectus Supplement

Prospectus

You should rely only on the information contained in, or incorporated by reference into, this prospectus supplement, the accompanying prospectus or any free writing prospectus we deliver to you. Neither we nor the underwriters have authorized anyone to provide you with different information, and we and the underwriters do not take any responsibility for, and can provide no assurance as to the reliability of, any information that others may provide you. Neither we nor the underwriters are making an offer of these securities in any jurisdiction where the offer is not permitted. You should not assume that the information contained in this prospectus supplement, the accompanying prospectus or any free writing prospectus is accurate on any date other than the date set forth on the front of the document or that any information we have incorporated by reference in this prospectus supplement or the accompanying prospectus is accurate on any date other than the date of the applicable document incorporated by reference.

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a registration statement on Form S-3 that we initially filed with the U.S. Securities and Exchange Commission (the "SEC") on May 7, 2018 using a "shelf" registration process as a "well-known seasoned issuer," as defined in Rule 405 under the Securities Act of 1933, as amended (the "Securities Act").

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of our common stock and adds to and updates the information contained in the accompanying prospectus. The second part, the accompanying prospectus, 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. This prospectus supplement contains information about the common stock offered hereby and may add to, update or change information in the accompanying prospectus. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus, you should rely on the information in this prospectus supplement.

Before buying any of the shares of common stock offered hereby, we urge you to read carefully this prospectus supplement and the accompanying prospectus, together with the additional information described in the section entitled "Where You Can Find More Information; Incorporation of Certain Information by Reference."

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where it is lawful to do so. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy any shares other than the registered shares to which it relates, nor does this prospectus constitute an offer to sell or the solicitation of an offer to buy shares in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

This prospectus supplement and the accompanying prospectus contain summaries of certain provisions contained in some of the documents described herein and therein, 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 the documents referred to herein have been filed, or will be filed or incorporated by reference as exhibits to the registration statement, and you may obtain copies of those documents as described below under "Where You Can Find More Information; Incorporation of Certain Information by Reference."

Unless the context otherwise requires, references in this prospectus to "we," "us," "our," or the "Company" refer to AxoGen, Inc. and its wholly owned subsidiaries, AxoGen Corporation and AxoGen Europe GmbH.

This prospectus includes trademarks, tradenames and service marks that are the property of us and of other organizations. Solely for convenience, trademarks, trade names and service marks referred to in this prospectus may appear without the "™," "®," "©" or "SM" symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks, trade names and service marks. We do not intend our use or display of other parties' trademarks, trade names or service marks to imply, and such use or display should not be construed to imply, a relationship with, or endorsement or sponsorship of us by, these other parties.

PROSPECTUS SUPPLEMENT SUMMARY

This summary description about us and our business highlights selected information contained elsewhere in, or incorporated by reference into, this prospectus supplement or the accompanying prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should carefully read this entire prospectus supplement and the accompanying prospectus, including each of the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, before making an investment decision.

Overview

We are a global leader in innovative surgical solutions for physical damage or discontinuity to peripheral nerves. We provide products and education to improve surgical treatment algorithms for peripheral nerve damage or discontinuity. Our portfolio of products includes Avance Nerve Graft, an off-the-shelf processed human nerve allograft for bridging severed peripheral nerves without the comorbidities associated with a second surgical site, AxoGuard Nerve Connector, a porcine submucosa extracellular matrix ("ECM") coaptation aid for tensionless repair of severed peripheral nerves, AxoGuard Nerve Protector, a porcine submucosa ECM product used to wrap and protect injured peripheral nerves and reinforce the nerve reconstruction while preventing soft tissue attachments, and Avive Soft Tissue Membrane, a minimally processed human umbilical cord membrane that may be used as a resorbable soft tissue covering to separate tissues and modulate inflammation in the surgical bed. Along with these core surgical products, we also offer the AxoTouch Two-Point Discriminator and AcroVal Neurosensory and Motor Testing System. These evaluation and measurement tools assist healthcare professionals in detecting changes in sensation, assessing return of sensory, grip and pinch function, evaluating effective treatment interventions, and providing feedback to patients on peripheral nerve function. Our portfolio of products is available in the United States, Canada, the United Kingdom and several European and other international countries.

We began marketing products in 2008 and our revenues have increased from approximately $4.8 million in 2011 to approximately $60.4 million in 2017. Revenues for the three months ended March 31, 2018 were $17.3 million. Gross profit for the year ended December 31, 2017 and the three months ended March 31, 2018 were approximately $51.1 million and $14.5 million, respectively, while our losses from operations for the year ended December 31, 2017 and the three months ended March 31, 2018 were approximately $8.0 million and $5.0 million, respectively. We have continued to broaden our sales and marketing focus, which we expect to have a continuing positive contribution to our revenue growth in the long term.

Avance Nerve Graft and Avive Soft Tissue Membrane are processed in the United States at our processing facility in Dayton, Ohio. AxoGuard Nerve Connector and AxoGuard Nerve Protector are manufactured in the United States by Cook Biotech Incorporated ("Cook Biotech") and are exclusively distributed by us worldwide. The AcroVal Neurosensory and Motor Testing System and AxoTouch Two Point Discriminator are contract manufactured by Viron Technologies, LLC (formerly Cybernetics Research Laboratories) ("Viron") in Tucson, Arizona. Viron supplies the AcroVal Neurosensory and Motor Testing System and AxoTouch Two Point Discriminator unpackaged and they are packaged at our distribution facility in Burleson, Texas.

Peripheral Nerve Regeneration Market Overview

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

We believe the Avance Nerve Graft reduces overall procedure costs and may allow the use of cheaper local or regional anesthesia versus general anesthesia. It also prevents costs associated with potential

complications from the nerve autograft procedure given that surgical site infections at harvest site, may exceed $20,000 per case. Further, it may eliminate costs of increased hospitalization due to SSI, 9.7 days on average.

Every day patients suffer traumatic bodily injuries resulting in damage or discontinuity to peripheral nerves severe enough to require surgical treatment, including injuries from motor vehicle accidents, power tool injuries, gunshot wounds, dislocations, fractures, lacerations, or other forms of penetrating trauma. The peripheral nerves commonly damaged or discontinued from these traumas include the digital, median, ulnar, radial, facial, spinal accessory and brachial plexus nerves. The "Extremity Trauma" portion of the Market (as defined below) encompasses the traumatic PND described above but excludes the OMF, Breast and Carpal Tunnel (as such terms are defined below) portions of the Market.

Beyond the physical damage or discontinuity to peripheral nerves resulting from traumatic bodily injury described above, peripheral nerve damage or discontinuity also occurs due to surgical intervention. Nerve damage or discontinuity can occur during dental and oral surgery procedures such as third molar extractions, placement of dental implants and removal of tumors during which one or more sections of the trigeminal nerve can be damaged or discontinued ("OMF"). This can result in numbness in certain areas of the face and mouth.

Breast reconstruction neurotization ("Breast") is another portion of the Market. Currently, when a woman undergoes autologous breast reconstruction after a mastectomy, she receives the shape of a natural breast but loses sensory feeling. This forfeiture of sensation can have a profound effect contributing to quality of life issues such as depression and other emotional challenges. In certain cases, sensation can be returned to the breast area with the use of the Company's products through an innovative surgical technique called ReSensation™. The Company believes that the ideal breast reconstruction should restore size, shape, symmetry, softness and now, sensation — without the potential risks and co-morbidity associated with autograft. The ReSensation™ technique incorporates the Company's vision into a reproducible and efficient solution for reconstructive plastic surgeons.

Finally, peripheral nerves can also be damaged due to compression injuries. For instance, severe and recurrent carpal tunnel cases may result in complications and damage to the peripheral nerve that requires surgical intervention and protection of the peripheral nerve. PND caused by recurrent carpal tunnel syndrome and cubital tunnel syndrome constitutes the "Carpal Tunnel" portion of the Market.

We estimate the United States PND market for our current product portfolio for Extremity Trauma, OMF, Breast and Carpal Tunnel is $2.2 billion (the "Market"). From a product prospective, as to the Market, we estimate that Avance Nerve Graft represents $976 million, AxoGuard Nerve Connector represents $391 million, AxoGuard Nerve Protector represents $433 million and Avive Soft Tissue Membrane represents $439 million.

We estimate that the Extremity Trauma portion of the Market is approximately $1.5 billion. The estimated size of the Extremity Trauma portion of the market is based upon epidemiological studies regarding the general number of trauma patients, physician interviews and incidence of PND in the population. We believe that each year in the U.S. more than 1.4 million people suffer damage or discontinuity to peripheral nerves resulting in over 700,000 extremity nerve repair procedures.

We estimate that the OMF portion of the Market is approximately $293 million, based upon research that has indicated approximately 80,350 PND occur in the U.S. each year that are related to benign tumor resections, third molar surgeries, anesthetic injections and dental implants. We have applied the average sales price of the Avance Nerve Graft, AxoGuard Nerve Connector and AxoGuard Nerve Protector that address such PND in order to derive the OMF portion of the Market.

According to market data, there are annually 307,660 breast cancer patients of which 113,834 receive a mastectomy. Of those mastectomy patients, every year, more than 20,000 women choose autologous flap

reconstruction as compared to implant based reconstructions. Removing those procedures that are not appropriate for neurotization, and based upon our assumption that 65% of women will elect to have a bilateral procedure, we estimate that the Breast portion of the Market is approximately $250 million.

We estimate that the Carpal Tunnel portion of the Market is approximately $188 million, or 118,000 procedures. According to literature, there are approximately 500,000 primary carpal tunnel and 53,000 primary cubital tunnel relief surgeries performed annually in the U.S. For carpal tunnel, we estimate that our addressable market is the 20% of carpal tunnel surgeries that require revision procedures to address the recurrence of symptoms. From the 53,000 primary cubital tunnel surgeries, we estimate that our addressable market is 18,000 of such surgeries comprised of revision and primary interventions. As a result, we estimate that approximately 100,000 carpal tunnel revision surgeries and 18,000 total cubital tunnel procedures are addressable each year in the U.S. to mitigate the recurrence of symptoms. These revision and primary surgeries are required due to compression of the peripheral 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 procedures.

Market Expansion Opportunities

Although distribution and sales of products in the Extremity Trauma, OMF, Breast and Carpal Tunnel portions of the Market constitute our prime revenue sources today, market expansion opportunities in lower extremity surgery, head and neck surgery, urology and the surgical intervention for pain offer us new and expanded revenue opportunities. For example, we have developed the AxoGuard NerveCap which is designed to protect a peripheral nerve end and separate the nerve from the surrounding environment to reduce the development of asymptomatic or painful neuromas ("Neuroma Management"). A neuroma is a tangled mass of disorganized nerve and fibrous tissue which, if not properly diagnosed and addressed, can require long term pharmacologic treatment and pain management. An example of the use of the AxoGuard Nerve Cap is in the situation of a digital amputation whereby the nerves that are cut in the amputation may form a neuroma if the nerve end is not properly terminated or capped. We intend in 2018 to conduct clinical evaluation and user preference studies of the AxoGuard Nerve Cap and define our marketing plan for Neuroma Management.

Lower limb/total join replacement is another market opportunity. In the United States there are approximately 700,000 total knee replacements ("TKR") per year and 310,000 total hip replacements ("THR") per year. We estimate that 6% of patients have neuropathic pain with TKR and THR and more than 60,000 have neuropathic pain post joint replacement. We believe if we proceed with entering this area in the future it would increase the market for our products by approximately $125 million.

Corporate Information

We were incorporated in Minnesota in 1977. Our principal offices are located at 13631 Progress Boulevard, Suite 400, Alachua, Florida 32615. Our telephone number is (386) 462-6800. We have two wholly owned subsidiaries, AxoGen Corporation, a Delaware corporation, and AxoGen Europe GmbH, a limited liability corporation with its corporate seat in Vienna, Austria. Our web address is *www.axogeninc.com*. Information contained in, or accessible through, our website does not constitute a part of this prospectus.

Our reports that have been filed with the SEC are available on our website free of charge, including our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, Forms 3, 4 and 5 filed on behalf of directors and executive officers and any amendments to such reports filed pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Copies of this prospectus supplement and the accompanying prospectus may also be obtained without charge electronically or by paper by contacting Investor Relations, c/o AxoGen, Inc., 13631 Progress Boulevard, Suite 400, Alachua, Florida 32615 or by calling (386) 462-6800.

THE OFFERING

Common stock offered by us	3,000,000 shares, plus up to an additional 450,000 shares if the underwriters exercise in full their option to purchase additional shares.
Common stock to be outstanding immediately after this offering	37,669,276 shares, or 38,119,276 shares if the underwriters exercise in full their option to purchase additional shares.
Underwriters' option to purchase additional shares	We have granted the underwriters an option to purchase up to an aggregate of 450,000 additional shares of our common stock, at the public offering price, less the underwriting discounts and commissions. The option is exercisable, in whole or in part, for a period of 30 days following the date of this prospectus supplement.
Use of proceeds	We currently intend to use the net proceeds from the sale of the shares sold by us in this offering for long-term facility and capacity expansion and general corporate purposes. See "Use of Proceeds" in this prospectus supplement.
Risk factors	Investing in our common stock involves a high degree of risk. See risk factors described under the caption "Risk Factors" in this prospectus supplement, as well as the other information set forth in this prospectus supplement and the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, for a discussion of factors that you should carefully consider before deciding to invest in our common stock.
Nasdaq Capital Market symbol	AXGN.

The number of shares of common stock to be outstanding after this offering is based on 34,669,276 shares outstanding on March 31, 2018, and excludes:

- 4,057,175 shares of common stock issuable upon the exercise of options outstanding as of March 31, 2018, at a weighted average exercise price of $7.87 per share;
- 654,505 shares of common stock subject to vesting of performance stock units and restricted stock unit awards outstanding as of March 31, 2018;
- 1,437,173 shares of common stock available for future issuance as of March 31, 2018 under our AxoGen 2010 Stock Incentive Plan, as amended and restated (the "Stock Incentive Plan"); and
- 600,000 shares of common stock available for future issuance as of March 31, 2018 under our AxoGen 2017 Employee Stock Purchase Plan (the "2017 ESPP").

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of outstanding options after March 31, 2018, and no exercise by the underwriters of their option to purchase additional shares of our common stock from us.

RISK FACTORS

An investment in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information set forth in this prospectus supplement and the accompanying prospectus, and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, before deciding to purchase shares of our common stock. If any of the events, contingencies, circumstances or conditions described in the risks below actually occurs, our business, financial condition or results of operations could be seriously harmed. The trading price of our common stock could, in turn, decline and you could lose all or part of your investment.

Risks Related To The 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 revenue from distribution of its products, which may not be achievable.

AxoGen has historically operated with negative cash flow from its operations. As of December 31, 2017, AxoGen had an accumulated deficit of approximately $128 million. If AxoGen's revenue does not increase as anticipated, then AxoGen will continue to experience negative cash flows and adverse operating conditions. AxoGen's continuing capital needs and other factors could cause it 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 distribution and 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 distribution and sales channels composed of a combination of its direct sales force and independent distributors to allow it to increase distribution and sales to existing customers and reach new customers. There can be no assurance that these efforts will be successful in expanding AxoGen's revenue. AxoGen currently distributes tissue and sells products directly through its employees and indirectly through distributor relationships. AxoGen is engaged in an 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 attract new customers, it may not be able to grow revenue or maintain its current level of revenue generation.

AxoGen's revenue depends primarily on four products.

Substantially all of AxoGen's revenue is currently derived from only four products, the Avance Nerve Graft, Avive Soft Tissue Membrane, AxoGuard Nerve Protector and AxoGuard Nerve Connector, for the treatment of peripheral nerve damage. Of these four products, the Avance Nerve Graft represents approximately half of the AxoGen's total revenues. Any disruption in AxoGen's ability to generate revenue from the distribution of tissue and sale of products will have a material adverse impact on AxoGen's business, results of operations, financial condition and growth prospects.

The AxoGuard products are only available through an exclusive distribution agreement with Cook Biotech. The agreement was amended February 26, 2018 to run through June 30, 2027. 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 obtained through the agreement with Cook Biotech, 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.

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 and provide appropriate solutions for nerve repair. 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 products and negatively impact the supply of available donor tissue.

AxoGen is highly dependent on its ability to recover human tissue from tissue donors for its Avance Nerve Graft product and Avive Soft Tissue Membrane. 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 tissue, including bones and tendons, may limit widespread acceptance of AxoGen's Avance Nerve Graft and Avive Soft Tissue Membrane. 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 and donated tissue use. 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 or donors themselves 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 licenses from Community Blood Center (d/b/a Community Tissue Services) ("CTS"), 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 CTS facility service agreement which can occur upon 18 months' prior 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 service facilities takes 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 service agreement 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 processing of its products.

AxoGen's Avance Nerve Graft is processed through its Avance Process which requires careful calibration and precise, high-quality processing and manufacturing. Its Avive Soft Tissue Membrane is also human tissue that requires skill in its processing. Achieving precision and quality control requires skill and diligence by its personnel. If it fails to achieve and maintain these high levels of quality control and processing standards, including avoidance of processing 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 processing of its Avance and Avive products, 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 human tissue products 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.

Delays, interruptions or the cessation of production by AxoGen's third party suppliers of important materials or delays in qualifying new materials, may prevent or delay AxoGen's ability to manufacture or process the final products.

Most of the raw materials used in the process for Avance Nerve Graft and Avive Soft Tissue Membrane are available from more than one supplier. However, one of the chemicals AxoGen uses in the processing of Avance Nerve Graft is no longer manufactured by the original single source provider. AxoGen has inventory of such chemical which it believes provides more than one year of production. AxoGen is completing evaluation of multiple avenues including new suppliers 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. AxoGen does not have written contracts with any of its single source suppliers, and at any time they could stop supplying AxoGen's orders. U.S. Food and Drug Administration (the "FDA"), approval of a new supplier may be required if these materials become unavailable from AxoGen's current 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 process tissue. 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.

The failure of third parties to perform many necessary services for the commercialization of Avance Nerve Graft and Avive Soft Tissue Membrane, including services related to recovery, distribution and transportation, would impair AxoGen's ability to meet commercial demand.

AxoGen relies upon third parties for certain recovery, distribution and transportation services. In accordance with product specifications, 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 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 revenue 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 AxoGen is unable to establish new distribution relationships or renew current distribution agreements on commercially acceptable terms, its 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 or scale its operations.

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 or maintain pricing without significant discounting, 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 and/or surgeon 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.

Currently, certain reimbursement coding and coverage is in place for nerve repair and grafting. CMS announced new CPT codes for nerve allograft, effective January 1, 2018 (CMS-1676-F). Nerve Repair, with nerve allograft, each nerve, first strand (cable), is CPT: 64912, and Nerve Repair with nerve allograft, each additional strand, is CPT: 64913. These new CPT codes are the result of approval by the American Medical

Association and CPT Advisory Committee and reflect clinical evidence supporting Avance® processed nerve allograft. Medicare reimbursement for hospital in-patient ranges from approximately $11,514 - $22,948.

AxoGen may be subject to future product liability litigation which 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. Although AxoGen currently carries product liability insurance in an amount consistent with industry averages, 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, commercially available wraps and amnion products, 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. Amnion products are widely available and AxoGen may not be able to distinguish the Avive Soft Tissue Membrane from such other products so as to produce significant revenue from its distribution. Also, steady improvements have been made in synthetic human tissue substitutes, which could compete with AxoGen's products in the future. 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 AxoGen's products rendering AxoGen's products 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 certain countries outside the U.S. AxoGen intends to expand distribution and sales in these and other countries outside the U.S. and will need to comply with applicable foreign regulatory requirements, including obtaining the requisite approvals to do so. Avive Soft Tissue Membrane is only available in the U.S. and has not, as of this time period, received any regulatory registration allowing for distribution outside the U.S. 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 revenue 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, implants 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, the effective recovery of tissue, the timely receipt, recording, review and approval of required medical and testing 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 costs.

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. Finally, AxoGen can provide no assurance that it can keep inventory costs within its target levels. Failure to do so may harm long term growth prospects.

AxoGen's payment obligations under the MidCap Financial Trust Term Loan Agreement and Revolving Loan Agreement may adversely affect AxoGen's financial position and AxoGen's ability to obtain additional funds, and may increase AxoGen's vulnerability to economic or business downturns.

On October 25, 2016 (the "Closing Date"), AxoGen and AC, each as borrowers, entered into the term loan agreement (the "MC Term Loan Agreement") with the lenders party thereto and MidCap Financial Trust ("MidCap"), as administrative agent and lender. Under the MC Term Loan Agreement, MidCap provided AxoGen a term loan in the aggregate principal amount of $21 million (the "Term Loan"). On the Closing Date, AxoGen and AC, each as borrowers, also entered into a Credit and Security Agreement (Revolving Loan) (the "'Revolving Loan Agreement") with the lenders party thereto and MidCap, as administrative agent and a lender. Under the Revolving Loan Agreement, MidCap has agreed to lend AxoGen up to $10 million under a revolving credit facility (the "Revolving Loan") which amount may be drawn down by AxoGen based upon an available borrowing base. The Revolving Loan may be increased to up to $15 million at AxoGen's request and with the approval of MidCap. As of March 31, 2018, AxoGen's borrowing base under the Revolving Loan provided availability of approximately $7.9 million and had an outstanding balance of $4 million. The MC Term Loan Agreement, Revolving Loan Agreement and the indebtedness pursuant thereto are secured by substantially all of AxoGen's tangible and intangible assets.

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

- a portion of AxoGen's cash flow from operations will be needed to pay debt service and will not be available to fund future operations;
- AxoGen is required to maintain certain covenants, the breach of which would result in default under the MC Term Loan Agreement and Revolving Loan Agreement;
- AxoGen has increased vulnerability to adverse general economic and industry conditions; and
- AxoGen may be vulnerable to higher interest rates because interest expense on the Term Loan in limited circumstances could increase.

Payment requirements under the MC Term Loan Agreement and the Revolving Loan Agreement increase AxoGen's cash burden. AxoGen's future operating performance is subject to market conditions and business factors that are beyond its control. If AxoGen's cash flows and capital resources are insufficient to allow

AxoGen to make required payments, AxoGen may have to reduce or delay capital expenditures, sell assets, seek additional capital or restructure or refinance its debt. If AxoGen raises funds by selling additional equity, such sale would result in dilution to its shareholders. There is no assurance that if AxoGen is required to secure funding it can do so on terms acceptable to it, or at all. Failure to pay interest or the principal amount when due would result in a default under the MC Term Loan Agreement and Revolving Loan Agreement and result in foreclosure on AxoGen's assets which would have a material adverse effect.

The MC Term Loan Agreement and Revolving Loan Agreement each contain certain covenants and failure to comply with the terms of such indebtedness could result in a default that could have material adverse consequences for us.

The MC Term Loan Agreement and the Revolving Loan Agreement each contain covenants that place restrictions on AxoGen's operations, including, without limitation, covenants related to debt restrictions, investment restrictions, dividend restrictions, restrictions on transactions with affiliates and certain revenue covenants. AxoGen's ability to comply with these covenants may be affected by general economic and industry conditions, as well as market fluctuations and other events beyond AxoGen's control. AxoGen does not know if it will be able to satisfy all such covenants in the future. AxoGen's breach of the covenants could result in a default under such agreements. In the event of a default under such agreements, the lender could require AxoGen to repay some of its outstanding debt prior to maturity, and/or to declare all amounts borrowed by it, together with accrued interest, to be due and payable. In the event that this occurs, AxoGen may be unable to repay all such accelerated indebtedness. Any indebtedness that it incurs under the MC Term Loan Agreement and Revolving Loan Agreement is secured by substantially all of its tangible and intangible assets. If AxoGen defaults under the indebtedness secured by its assets, those assets would be available to the secured creditors to satisfy AxoGen's obligations to the secured creditors. As of March 31, 2018, AxoGen was in compliance with the loan covenants.

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

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.

AxoGen's business and stock price may be adversely affected if AxoGen's internal controls are not effective.

Section 404 of the Sarbanes-Oxley Act of 2002 requires that public companies 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 it.

In our annual report on Form 10-K for the year ended December 31, 2016, we reported material weaknesses in our internal control as of December 31, 2016 relating to the design and operation of key controls around the calculations of significant judgment and estimates and quarterly cycle count procedures related to consigned inventories. These control deficiencies did not result in any changes of prior period financial statements or previously released financial results. We believe we took appropriate actions to remediate the control deficiencies we identified in these instances.

Although we have taken actions to correct 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 (such as hurricanes and other natural 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. 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, privacy laws, and anti-bribery laws such as the United States Foreign Corrupt Practices Act. For example, the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, (e.g. compensation payments, subsidization of marketing activities) to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a U.S. healthcare program such as Medicare and Medicaid. The False Claims Act imposes penalties against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used by, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. government. 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 ("DOJ"), 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. There can also be changes to the regulations by foreign and domestic government entities that require AxoGen to update or upgrade business processes or to perform additional validation activities for product or processes. Compliance with such changes can be costly to implement or result in non-compliance and restricting the ability to distribute tissue or sell products that would have a material adverse effect.

Our products are also subject to regulation by the FDA in the U.S. The FDA regulates the development, clinical testing, marketing, distribution, manufacturing, labeling, import, export, advertising and promotion of biological products, such as that of AxoGen's Avance Nerve Graft product, and medical devices, for example the AxoGuard products. The Avive Soft Tissue Membrane is processed and distributed in accordance with FDA requirements for Human Cellular and Tissue-based Products ("HCT/Ps") under 21 CFR Part 1271 regulations, as well as U.S. State regulations. The FDA requires the approval of a biological

product, like the Avance Nerve Graft product, through a biologic license application ("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 Federal Food, Drug and Cosmetic Act ("FD&C Act"), the current good manufacturing practice ("cGMP") regulations in 21 CFR Parts 210 and 211 and the applicable regulations and standards in 21 CFR Parts 600-610 prior to submission of a BLA for the Avance Nerve Graft; (2) conducts a phase 3 clinical trial to demonstrate safety, purity and potency of the Avance Nerve Graft under a Special Protocol Assessment; (3) continues to comply with the requirements of 21 CFR Part 1271 for HCT/Ps; and (4) exercises due diligence in executing the transition plan. See "Business — Government Regulations — U.S. Government Regulation Review" of AxoGen's annual report on Form 10-K for the fiscal year ended December 31, 2017.

In the FDA's regulation of medical devices, the FDA requires 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. Our current and future marketing activities and business practices such as co-marketing activities with hospitals, healthcare facilities, or other potential customers, including any provision coverage, coding and reimbursement information on our products or procedures using our products, is similarly subject to regulation under the US Fraud and Abuse Laws such as the Anti-Kickback Statute and False Claims Act. See "Business — Government Regulations — Education Grants, U.S. Anti-kickback, False Claims and Other Healthcare Fraud and Abuse Laws — Fraud, Abuse and False Claims".

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 the transition plan for AxoGen's Avance Nerve Graft will ultimately result in 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. Furthermore, the FDA could limit or prevent the distribution of AxoGen products and the FDA 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 existing clearances and approvals along with applicable cGMP regulations, including those relating to specifications, development, documentation, validation, testing, quality control and product labeling. A determination that AxoGen is in violation of such regulations or any of its product clearances or approvals 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 AxoGen 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 the FDA clearance. The Avive Soft Tissue Membrane is processed and distributed in accordance with FDA requirements for HCT/Ps under 21 CFR Part 1271 regulations and is to be dispensed only by or on the order of a licensed physician and is contraindicated for use in any patient in whom soft tissue implants are contraindicated. 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 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 suspension, debarment 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 Nerve Graft would have a material adverse effect on AxoGen.

The FDA considers 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 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. See "Business — Government Regulations — U.S. Government Regulation Review" of AxoGen's annual report on Form 10-K for the fiscal year ended December 31, 2017. AxoGen has continued to communicate with the FDA's Center for Biologics Evaluation and Research 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 effective investigational new drug application ("IND"). Subject to the FDA's enforcement discretion, AxoGen can commercially distribute the Avance Nerve Graft until the 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 the FDA changes its position for any reason regarding its use of enforcement discretion to permit AxoGen to distribute Avance Nerve Graft product in accordance with the transition plan, AxoGen would no longer be able to distribute Avance Nerve Graft, 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 business is subject to continuing compliance to standards by various accreditation and registration bodies which is costly and loss of accreditation or registration could result in negative effects on its business.

AxoGen is subject to accreditation such as that by the tissue bank industry's accrediting organization, American Association of Tissue Banks ("AATB"), and as a Verified-Accredited Wholesale Distributor. AxoGen has registration requirements such as that with the National Association of Boards of Pharmacy and ISO 13485 registration bodies. These accreditations and regulations can affect distribution and sale of AxoGen products on a state-by-state basis, within the United States and also affects distribution and sale of AxoGen products outside of the United States. The loss of accreditation or registration could keep AxoGen from selling and distributing its product which may have negative effects on its business.

AxoGen's AxoGuard® *and Avive 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 the AxoGuard product line and Cook Biotech is responsible for the regulatory compliance of the AxoGuard Connector and Protector product lines. 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 damage in which there is no gap or where a gap closure is achieved by flexion of the extremity. AxoGen is responsible for the regulatory compliance of the AxoGuard Nerve Cap. AxoGen has obtained a 510(k) premarket clearance for AxoGuard Nerve Cap to protect a peripheral nerve end and separate the nerve from the surrounding environment to reduce the development of symptomatic or painful neuroma. If AxoGen or Cook Biotech 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.

Avive Soft Tissue Membrane is processed and distributed in accordance with U.S. FDA requirements for Human Cellular and Tissue-based Products (HCT/P) under 21 CFR Part 1271 regulations, U.S. State regulations and the guidelines of the AATB. If AxoGen fails to comply with applicable regulatory requirements, the FDA could require AxoGen to stop providing Avive, or impose civil penalties, including fines, product seizures or product recalls and, in certain cases, criminal sanctions.

AxoGen's AxoTouch and AcroVal products are subject to FDA and other regulatory requirements.

AxoGen's AxoTouch and AcroVal products are regulated as medical devices 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. If AxoGen fails to comply with applicable regulatory requirements, the FDA could deny or withdraw 510(k) clearance for these 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 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. The 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, in such circumstances, the FDA usually initially 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, the 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 that may pose a risk to health. A government-mandated, government-requested or voluntary recall could occur as a result 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. See "Business — Regulation — Education Grants, U.S. Anti-kickback, False Claims and Other Healthcare Fraud and Abuse Laws — Fraud, Abuse and False Claims" of AxoGen's annual report on Form 10-K for the fiscal year ended December 31, 2017. 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 operations must comply with FDA and other governmental requirements.

AxoGen's 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. See "Business — Government Regulations — Education Grants, U.S. Anti-kickback, False Claims and Other Healthcare Fraud and Abuse Laws — Fraud, Abuse and False Claims" of AxoGen's annual report on Form 10-K for the fiscal year ended December 31, 2017. 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 revenue and its ability to generate profits. Furthermore, AxoGen's key material suppliers, licensors and or other contractors may not 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.

Distribution of AxoGen human tissue products outside the U.S. are subject to foreign regulatory requirements that vary from country to country. In the European Union ("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.

Distribution of AxoGen AxoGuard products are also subject to foreign regulatory requirements that vary from country to country. The primary regulatory body in Europe is the E.U. which has adopted numerous directives and promulgated voluntary standards regulating the design, manufacture and labeling of, and clinical trials and adverse event reporting for, medical devices. Devices that comply with the requirements of a relevant directive will be entitled to bear CE marking, indicating that the device conforms to the essential requirements of the applicable directives and, accordingly, can be commercially distributed throughout the member states of the E.U. and other countries that comply with these directives. The method for assessing conformity varies depending on the type and class of the device, but normally involves an assessment by the manufacturer and a third-party assessment by a notified body, an independent and neutral institution appointed by a country to conduct the conformity assessment.

Cook Biotech is responsible for all regulatory filings for the AxoGuard Connector and Protector products including international registrations such as CE marking. In April 2013 the AxoGuard Connector and Protector product lines were awarded the CE Mark allowing distribution into the E.U. and other countries that accept the CE Mark. In April 2018 the CE Mark for the AxoGuard products expired and Cook Biotech is seeking renewal. The Company believes that it has adequate inventory of the AxoGuard products in the EU so that sales are not disrupted while the renewal is obtained. While evaluating the CE renewal and inventory requirements, the Company decided to remove two AxoGuard product sizes from sale in the EU that did not meet its current sales objectives. It is continuing to evaluate if, or when, it will reintroduce such product sizes and if such reintroduction is to take place will pursue with Cook the CE Mark for these two products.

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. Although sales of AxoGuard products in the EU are not currently material, failure to obtain the CE Mark renewal in the EU would have a negative effect on the Company's ability to meet its future expansion goals in the EU.

In addition, the United Kingdom voted to exit the European Union ("Brexit") and the timing and scope remain unclear. AxoGen's current notified body for its CE Mark for AxoGuard products is in the United Kingdom. To date there is no business disruption, but AxoGen cannot be sure what changes could occur. If the notified body must change to an E.U. member there could be an interruption in sales in the E.U. Cost of regulatory compliance with both the United Kingdom and E.U. could be significant and time consuming.

Finally, regulations in both the United States and other countries are subject to constant change. There can be no assurance that AxoGen can meet the requirements of future regulations or that compliance with current regulations assures future capability to distribute and sell its products.

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 under FDA's statutory requirements 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 and received FDA approval to begin clinical testing in March 2015. The phase 3 clinical trial was initiated in the second quarter of 2015. Additionally, AxoGen was audited by the FDA at its processing facility in March 2013, March 2015 and October 2016 and its Distribution Facility in October 2015. 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. Final determination of regulatory compliance with 21 CFR Parts 210/211 and 600-610 will be made during FDA's pre-license inspection as part of the BLA review. If the 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 could not occur or be 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 on AxoGen's BLA 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 AxoGen 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 provide 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 nonclinical 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 ("cGMP") 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 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 and Avive Soft Tissue Membrane 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, as is the Avive Soft Tissue Membrane, 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/Ps. The first regulation requires that companies that produce and distribute HCT/Ps register with the FDA. The second regulation 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 regulation 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, the three basic requirements of 21 CFR Part 1271 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. In addition, new guidance was issued by the FDA in late 2017 on Regulatory Considerations for Human Cells, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use. FDA actions interpreting the guidance will need to be followed closely, and the potential implications on the regulatory status of Avive and future HCT/P products is being evaluated by the Company.

Additional regulations or guidance documents may be implemented by the FDA in the future. These changes may require new documentation requirements, process changes or testing that could increase costs and regulatory burden. See "Business — Government Regulations" of AxoGen's annual report on Form 10-K for the fiscal year ended December 31, 2017. These regulations can also increase the cost of tissue recovery activities. Finally, Avance Nerve Graft and Avive Soft Tissue Membrane are subject to certain state and local regulations, as well as compliance with the standards of the 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 and umbilical cord 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 and umbilical cord 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 other states, are particularly relevant to AxoGen's business. Most states do not currently have tissue banking regulations. However, incidents of allograft related issues in the industry may stimulate the development of regulation in other states. It is possible that third parties 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 (the "ACA"), 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. The ACA significantly impacts the biotechnology and medical device industries and could have a material adverse impact on numerous aspects of AxoGen's business.

The ACA includes, among other things, the following measures:

- 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, which has been suspended through 2019;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities and conduct comparative clinical effectiveness research;
- new reporting and disclosure requirements on certain medical device and pharmaceutical 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");
- an amendment to the intent requirement of the federal Anti-Kickback and criminal health care fraud statutes, so that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the false claims statutes;
- 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 biosimilar and interchangeable with a licensed biologic product.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. The current Presidential Administration and U.S. Congress have attempted and will likely continue to seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. It is uncertain the extent to which any such changes, if made, may impact our business or financial condition.

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 certain medical device and pharmaceutical 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 IP 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 IP, maintain trade secret protection, and conduct operations without violating or infringing on the IP rights of third parties. See "Business — Intellectual Property" of AxoGen's annual report on Form 10-K for the fiscal year ended December 31, 2017. 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;
- 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 our 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 enjoin 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 it 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, the material U.S. patents covering the formulations used in our AxoGuard product line, which are held by Cook Biotech, have expired. Expiration of these patents could adversely affect our ability to successfully execute our business strategy to maximize the value of AxoGuard products and could 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.

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 the University of Florida Research Foundation (the "UFRF") and the University of Texas at Austin ("UTA") where the original technologies are purported to have been invented. Though AxoGen makes an effort to follow these agreements strictly, a disagreement between AxoGen and either party could

have a negative impact on its ability to operate its business effectively. In addition, AxoGen could learn that the technologies it has licensed from UFRF and UTA do not perform as purported, are not efficacious, or are not the property of UFRF or UTA, or some similar problem with the license, any of which would have an immediate and negative impact on AxoGen's business.

AxoGen Trademarks are Valuable

In the U.S. and other countries, we currently hold issued trademark registrations and have trademark applications pending, any of which may be the subject of a governmental or third party objection, which could prevent the maintenance or issuance of the same. As our products mature, our reliance on our trademarks to differentiate us from our competitors increases and as a result, if we are unable to prevent third parties from adopting, registering or using trademarks and trade dress that infringe, dilute or otherwise violate our trademark rights, our business could be materially adversely affected.

Risks Related to Our Common Stock

An active trading market in our common stock may not be maintained.

The trading market in our common stock has been extremely volatile. The quotation of our common stock on the Nasdaq Capital Market does not assure that a meaningful, consistent and liquid trading market will exist. We cannot predict whether an active market for our common stock will be maintained in the future. An absence of an active trading market could adversely affect our shareholders' ability to sell our common stock at current market prices in short time periods, or possibly at all. Additionally, market visibility for our common stock may be limited and such lack of visibility may have a depressive effect on the market price for our common stock. As of March 31, 2018, approximately 24.60% of our outstanding shares of common stock was held by our officers, directors, beneficial owners of 5% or more of our securities and their respective affiliates, which adversely affects the liquidity of the trading market for our common stock, in as much as federal securities laws restrict sales of our shares by these shareholders. If our affiliates continue to hold their shares of common stock, there will be limited trading volume in our common stock, which may make it more difficult for investors to sell their shares or increase the volatility of our stock price.

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

Our common stock is listed on the Nasdaq Capital Market under the symbol "AXGN." The stock market in general, and the market for medical technology companies in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The trading price of our common stock 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 stock 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, including the other factors described in this "Risk Factors" section, 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 operation and expansion of our business will continue to require funding. In addition, the MC Term Loan Agreement and Revolving Loan Agreement prohibit us from paying cash dividends to our shareholders. Accordingly, we do not anticipate that we will pay any cash dividends on our common stock 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 any investor purchases shares of common stock, realization of a gain on such investment will depend on the appreciation of the price of our common stock, which may never occur. Investors seeking cash dividends in the foreseeable future should not purchase our common stock.

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 common stock at a premium over the market price.

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 stock, 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

Management will have broad discretion as to the use of the proceeds we receive from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds we receive from this offering, including for any of the purposes described in the section entitled "Use of Proceeds" of this prospectus supplement, and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially. Our management could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business and cause the price of our common stock to decline.

If you purchase shares of common stock in this offering, you will experience immediate and substantial dilution in the net tangible book value of your shares.

Investors purchasing shares of common stock in this offering will pay a price per share that substantially exceeds the as adjusted book value per share of our tangible assets as of March 31, 2018 after subtracting our liabilities. Our net tangible book value as of March 31, 2018 was approximately $20,633,000, or approximately $0.60 per share of our common stock. Based on the public offering price of $41.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of March 31, 2018 would have been approximately $135,752,936, or approximately $3.60 per share of our common stock.

This dilution is due to the substantially lower price paid by some of our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering, and the exercise of stock options granted to our employees. In addition, we have a significant number of stock options outstanding. The exercise of any of these options would result in additional dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. Further, because we will need to raise additional capital to fund our future activities, we may in the future sell substantial amounts of common stock or securities convertible into or exchangeable for common stock. Future issuances of common stock or common stock-related securities, together with the exercise of outstanding options, if any, may result in further dilution. For a further description of the dilution that you will experience immediately after this offering, see the section titled "Dilution" of this prospectus supplement.

Future sales of our common stock could cause our stock price to decline.

Sales of a substantial number of shares of our common stock in the public market following this offering, or the perception that these sales might occur, may reduce the prevailing market price of our common stock and make it more difficult for you to sell your common stock at a time and price that you deem appropriate. In addition, any sales of securities by us or existing shareholders could have a material adverse effect on the market price of our common stock.

For example, pursuant to a registration rights agreement between us and EW Healthcare Partners L.P., formerly named Essex Woodlands Fund IX, L.P. ("Essex"), we have filed a registration statement that registers for resale an aggregate of 4,861,111 shares of common stock held by Essex, of which shares Essex still holds 3,711,111. Shares held by Essex that remain unsold but covered by the registration statement are freely tradable without restriction under the Securities Act, subject to a contractual lockup agreement currently binding upon Essex which expires May 15, 2018. Our directors, executive officers and Essex have also entered into 90 day lockup agreements with the underwriters in connection with this offering, however two of our officers are permitted to sell an aggregate of 17,500 shares of our common stock in their sole discretion. See "Underwriting."

In addition, we may need to raise additional capital to fund our future activities. We may raise money through additional public or private offerings of our equity securities or equity-linked securities, or through other means. Any sales of our equity or equity-linked securities could have a material adverse effect on the market price of our common stock.

Further, we have a significant number of stock options outstanding. If a substantial number of shares of common stock underlying these options are sold, or if it is perceived that they will be sold, in the public market, it could have a material adverse effect on the market price of our common stock.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain statements contained in, or incorporated by reference into, this prospectus supplement or the accompanying prospectus constitute "forward-looking statements" within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act. All statements other than statements of historical fact may be deemed to be forward-looking statements. Forward-looking statements frequently, but not always, use the words "may," "estimate," "projects," "intends," "plans," "believes," "anticipates" or "expects" or similar words and may include statements concerning our strategies, goals and plans. Forward-looking statements may include, without limitation, statements regarding our assessment on our internal control over financial reporting, our growth, our earnings guidance, product development, product potential, financial performance, sales growth, product adoption, market awareness of our products, data validation and our visibility at, and sponsorship of, conferences and educational events.

All forward-looking statements are based on management's present expectations of future events and are subject to a number of assumptions that could cause actual results to differ materially from those described in the forward-looking statements. Forward-looking statements should be evaluated together with the many risks and uncertainties that affect our business and market, including those risks and uncertainties discussed in the following documents:

- the risk factors contained in this prospectus supplement under the caption "Risk Factors";
- our most recent annual report on Form 10-K, including the sections entitled "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations";
- our quarterly reports on Form 10-Q; and
- our other SEC filings.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in, or incorporated by reference into, this prospectus supplement or the accompanying prospectus might not occur. Investors are cautioned not to place undue reliance on the forward-looking statements, which speak only of the date the statement is made. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements after the date on which the statement is made, whether as a result of new information, future events or otherwise, except as may be required by applicable law. All subsequent forward-looking statements attributable to us are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

USE OF PROCEEDS

At the public offering price of $41.00 per share, we expect to receive net proceeds of approximately $115,120,000 in this offering, or $132,463,000 if the underwriters exercise in full their option to purchase additional shares, after deducting the underwriting discounts and commissions and estimated expenses payable by us. We currently intend to use the net proceeds from the sale of the shares sold in this offering for long term facilities and capacity expansion and general corporate purposes.

The expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures will depend on numerous factors. As a result, our management will have broad discretion in applying the net proceeds from this offering, and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially. Our management could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock.

MARKET PRICE OF OUR COMMON STOCK

The following table shows, for the periods indicated, the high and low bid sales per share of our common stock as reported by Nasdaq.

	High	Low
2016		
First quarter	$ 5.60	$ 4.52
Second quarter	$ 6.88	$ 4.90
Third quarter	$ 9.88	$ 6.41
Fourth quarter	$ 9.28	$ 7.65
2017		
First quarter	$ 11.25	$ 8.75
Second quarter	$ 16.90	$ 10.05
Third quarter	$ 19.45	$ 14.30
Fourth quarter	$ 28.90	$ 18.10
2018		
First quarter	$ 40.95	$ 23.60
Second quarter (through May 8, 2018)	$ 43.96	$ 34.80

On May 8, 2018, the last reported sale price of our common stock on Nasdaq was $43.35 per share. As of May 4, 2018, there were approximately 269 holders of record, based upon information received from our stock transfer agent. However, this number does not include beneficial owners whose shares were held of record by nominees or broker dealers. The Company estimates that there are more than 8,800 individual owners.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain our future earnings, if any, for use in our business and therefore do not anticipate paying cash dividends in the foreseeable future. Payment of future dividends, if any, will be at the discretion of our Board of Directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs and plans for expansion.

DILUTION

Investors purchasing shares of our common stock in this offering will suffer immediate and substantial dilution in the net tangible book value per share of common stock.

Our net tangible book value as of March 31, 2018 was approximately $20,633,000, or $0.60 per share of common stock. Net tangible book value per share is calculated by subtracting our total liabilities less the contingent consideration from our total tangible assets, which is total assets less intangible assets and goodwill, and dividing this amount by the number of shares of common stock outstanding.

After giving effect to the sale of 3,000,000 shares of our common stock at the public offering price of $41.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our net tangible book value as of March 31, 2018 would have been $135,752,936, or $3.60 per share of common stock. This represents an immediate increase in the net tangible book value of $3.00 per share to our existing shareholders and an immediate and substantial dilution in net tangible book value of $37.40 per share to new investors.

The following table, in conjunction with the preceding paragraph, illustrates this per share dilution:

Public offering price per share		$ 41.00
Historical net tangible book value per share as of March 31, 2018	$ 0.60	
Increase per share attributable to new investors	$ 3.00	
As adjusted net tangible book value per share after this offering		$ 3.60
Dilution per share to investors in this offering		$ 37.40

The information above assumes that the underwriters do not exercise their option to purchase additional shares. If the underwriters exercise in full their option to purchase additional shares, the as adjusted net tangible book value after this offering would increase to approximately $4.02 per share, representing an increase to existing shareholders of approximately $3.42 per share, and there would be an immediate dilution of approximately $36.98 per share to new investors in this offering.

The information in the above table is based on 34,669,276 shares outstanding on March 31, 2018, and excludes:

- 4,057,175 shares of common stock issuable upon the exercise of options outstanding as of March 31, 2018, at a weighted average exercise price of $7.87 per share;
- 654,505 shares of common stock subject to vesting of performance stock units and restricted stock unit awards outstanding as of March 31, 2018;
- 1,437,173 shares of common stock available for future issuance as of March 31, 2018 under the Stock Incentive Plan; and
- 600,000 shares of common stock available for future issuance as of March 31, 2018 under the 2017 ESPP.

To the extent that any of these outstanding options are exercised, any of these restricted stock units or performance stock units vest, or we issue additional shares under the Stock Incentive Plan or 2017 ESPP, there will be further dilution to new investors. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. The issuance of these securities could result in further dilution to new investors.

CAPITALIZATION AND INDEBTEDNESS

The following table describes our unaudited cash and cash equivalents, the current portion of liabilities and total capitalization as of March 31, 2018:

- on an actual basis; and
- on an as adjusted basis to give effect to the sale of 3,000,000 shares of common stock offered by us at the public offering price of $41.00 per share after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table in conjunction with the section of this prospectus supplement captioned "Use of Proceeds" as well as our "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements, including the related notes, incorporated by reference in this prospectus supplement and the accompanying prospectus, and in our annual report on Form 10-K for the year ended December 31, 2017 and our quarterly report on Form 10-Q for the fiscal quarter ended March 31, 2018.

	As of March 31, 2018	
	Actual	As Adjusted
	(unaudited, in thousands except share and per share data)	
Cash and cash equivalents	$ 30,560	$ 145,680
Total current liabilities	$ 15,567	$ 15,567
Long-term Obligations, net of current maturities and deferred financing fees[1]	$ 17,913	$ 17,913
Shareholders' equity:		
Common stock, $0.01 par value; 50,000,000 shares authorized (actual and as adjusted); 34,669,276 shares issued and outstanding (actual), 37,669,276 shares issued and outstanding (as adjusted)[2]	347	377
Additional paid-in capital[3]	155,312	270,402
Accumulated deficit	(133,968)	(133,968)
Total shareholders' equity	21,691	136,811
Total liabilities and shareholders' equity	$ 55,171	$ 170,291

(1) On October 25, 2016, AxoGen and AxoGen Corporation, each as borrowers, entered into a term loan agreement with MidCap Financial Trust, for a total of $21,000,000, net of $493,437 of unamortized deferred financing fees at March 31, 2018, and $554,100 at December 31, 2017. The loan has a fifty-four month term and requires interest only payments for the first twenty-four months, and thereafter, thirty monthly payments of principal and interest until the end of the term. Interest is payable monthly at 8.00% per annum plus the greater of LIBOR or 0.5% which as of March 31, 2018, resulted in a 9.66% rate.

(2) AxoGen had 34,669,276 shares outstanding on March 31, 2018, excluding: (i) 4,057,175 shares of common stock issuable upon the exercise of options outstanding as of March 31, 2018 at a weighted average exercise price of $7.87 per share, (iii) 654,505 shares of common stock subject to vesting of performance stock units and restricted stock unit awards outstanding as of March 31, 2018, (iv) 1,437,173 shares of common stock available for future issuance as of March 31, 2018 under the Stock Incentive Plan and (v) 600,000 shares of common stock available for future issuance as of March 31, 2018 under the 2017 ESPP.

(3) As adjusted represents additional paid-in capital attributable to the sale by us of shares in this offering, net of estimated issuance costs of $500,000.

UNDERWRITING

Jefferies LLC and Leerink Partners LLC are acting as joint book-running managers for this offering and as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in the underwriting agreement among us and the underwriters, we have agreed to sell to each underwriter, and each underwriter has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite such underwriter's name below.

Underwriter	Number of Shares
Jefferies LLC	1,125,000
Leerink Partners LLC	1,125,000
William Blair & Company, L.L.C.	450,000
JMP Securities LLC	300,000
Total	3,000,000

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of the shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representative has advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of $1.48 per share. After the initial offering of the shares, the public offering price, concession or any other term of the offering may be changed by the representative.

The following table shows the public offering price, underwriting discounts and commissions and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares of our common stock.

		Total	
	Per Share	Without Option	With Option
Public offering price	$ 41.00	$ 123,000,000	$ 141,450,000
Underwriting discounts and commissions	$ 2.46	$ 7,380,000	$ 8,487,000
Proceeds, before expenses, to us	$ 38.54	$ 115,620,000	$ 132,963,000

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $500,000. We also have agreed to reimburse the underwriters for certain of their expenses, as set forth in the underwriting agreement.

Option to Purchase Additional Shares

We have granted the underwriters an option to purchase up to an aggregate of 450,000 additional shares of common stock, at the public offering price, less the underwriting discounts and commissions, for a period of 30 days following the date of this prospectus supplement. If the underwriters exercise such option, each underwriter will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares from us proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We and our executive officers and directors and Essex have agreed not to sell or transfer any common stock or securities convertible into or exchangeable or exercisable for common stock, for 90 days after the date of this prospectus supplement without first obtaining the written consent of Jefferies LLC and Leerink Partners LLC on behalf of the underwriters, however two of our officers are permitted to sell an aggregate of 17,500 shares of our common stock in their sole discretion. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell any common stock;
- sell any option or contract to purchase any common stock;
- purchase any option or contract to sell any common stock;
- grant any option, right or warrant for the sale of any common stock;
- otherwise dispose of or transfer any common stock;
- request or demand that we file a registration statement related to the common stock; or
- enter into any swap or other agreement or any transaction that transfers, in whole or in part, the economic consequence of ownership of any common stock, whether any such swap, agreement or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

Notwithstanding the foregoing, and subject to the conditions below, parties to the lock-up agreements may transfer shares of our common stock without the prior written consent of the representatives:

(i) as a *bona fide* gift or gifts;

(ii) to any trust for the direct or indirect benefit of the undersigned or the immediate family of the undersigned (for purposes of this lock-up agreement, "immediate family" shall mean any relationship by blood, marriage or adoption, not more remote than first cousin);

(iii) as a distribution or other transfer by a partnership to its partners (including limited partners) or former partners or by a limited liability company to its members or retired members or by a corporation to its stockholders or former stockholders or to any wholly-owned subsidiary of such corporation;

(iv) to the undersigned's affiliates or to any investment fund or other entity controlled or managed by the undersigned;

(v) pursuant to a qualified domestic relations order or in connection with a divorce settlement;

(vi) by will or intestate succession upon the death of the undersigned; or

(vii) to the Company in satisfaction of any tax withholding obligation;

provided, in each case, that any transferee of such shares sign a similar lock-up agreement for the balance of the lock-up period and in the case of transfers pursuant to clauses (i), (ii) and (iv)-(vii) (1) any such transfer shall not involve a disposition for value, (2) such transfer is not required to be reported with the Securities and Exchange Commission on Form 4 in accordance with Section 16 of the Exchange Act, and (3) the transferor does not otherwise voluntarily effect any public filing or report regarding such transfers (other than a filing on a Form 5 made after the expiration of the lock-up period).

The Nasdaq Capital Market Listing

Our common stock is listed on The Nasdaq Capital Market under the symbol "AXGN."

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representative may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option described above. The underwriters may close out any covered short position by either exercising their option or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters 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 the option granted to them. "Naked" short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the closing of the offering.

The underwriters may also 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 representative has repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the Nasdaq Capital Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters 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 any of the underwriters make any representation that the representative will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Some of the underwriters and certain of their affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us and our affiliates, for which they may in the future receive customary fees, commissions and expenses.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling Restrictions

Notice to Prospective Investors in the European Economic Area

Any distributor subject to MiFID II that is offering, selling or recommending the common stock is responsible for undertaking its own target market assessment in respect of the common stock and determining its own distribution channels for the purposes of the MiFID product governance rules under Commission Delegated Directive (EU) 2017/593, or the Delegated Directive. Neither we nor the underwriters make any representations or warranties as to a distributor's compliance with the Delegated Directive.

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive, or a Relevant Member State, an offer to the public of any shares of common stock which are the subject of the offering contemplated by this prospectus may not be made in that Relevant Member State except that an offer to the public in that Relevant Member State of any shares of common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- to any legal entity which is a "qualified investor" as defined in the Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the underwriters or the underwriters nominated by us for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares of common stock shall require us or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer shares of common stock to the public" in relation to the shares of common stock 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 shares of common stock to be offered so as to enable an investor to decide to purchase or subscribe to the shares of common stock,

as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Notice to Prospective Investors in Canada

A. Resale Restrictions. The distribution of common stock in Canada is being made only in the provinces of Ontario, Quebec, Alberta and British Columbia on a private placement basis exempt from the requirement that we prepare and file a prospectus with the securities regulatory authorities in each province where trades of these securities are made. Any resale of the common stock in Canada must be made under applicable securities laws which may vary depending on the relevant jurisdiction, and which may require resales to be made under available statutory exemptions or under a discretionary exemption granted by the applicable Canadian securities regulatory authority. Purchasers are advised to seek legal advice prior to any resale of the securities.

B. Representations of Canadian Purchasers. By purchasing common stock in Canada and accepting delivery of a purchase confirmation, a purchaser is representing to us and the dealer from whom the purchase confirmation is received that:

- the purchaser is entitled under applicable provincial securities laws to purchase the common stock without the benefit of a prospectus qualified under those securities laws as it is an "accredited investor" as defined under National Instrument 45-106 — *Prospectus Exemptions*;
- the purchaser is a "permitted client" as defined in National Instrument 31-103 — *Registration Requirements, Exemptions and Ongoing Registrant Obligations*;
- where required by law, the purchaser is purchasing as principal and not as agent; and
- the purchaser has reviewed the text above under Resale Restrictions.

C. Conflicts of Interest. Canadian purchasers are hereby notified that Jefferies LLC and Leerink Partners LLC are relying on the exemption set out in section 3A.3 or 3A.4, if applicable, of National Instrument 33-105 — *Underwriting Conflicts* from having to provide certain conflict of interest disclosure in this document.

D. Statutory Rights of Action. Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if the offering memorandum (including any amendment thereto) such as this document contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser of these securities in Canada should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

E. Enforcement of Legal Rights. All of our directors and officers as well as the experts named herein may be located outside of Canada and, as a result, it may not be possible for Canadian purchasers to effect service of process within Canada upon us or those persons. All or a substantial portion of our assets and the assets of those persons may be located outside of Canada and, as a result, it may not be possible to satisfy a judgment against us or those persons in Canada or to enforce a judgment obtained in Canadian courts against us or those persons outside of Canada.

F. Taxation and Eligibility for Investment. Canadian purchasers of common stock should consult their own legal and tax advisors with respect to the tax consequences of an investment in the common stock in their particular circumstances and about the eligibility of the common stock for investment by the purchaser under relevant Canadian legislation.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following is a summary of the material U.S. federal income tax consequences to a non-U.S. holder (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering as of the date hereof. Except where noted, this summary deals only with common stock that is held as a capital asset as defined for purposes of Section 1221 of the United States Internal Revenue Code of 1986, as amended (the "Code").

A "non-U.S. holder" means a person (other than a partnership, or entity or arrangement treated as a partnership for U.S. federal income tax purposes) that is not for U.S. federal income tax purposes, any of the following:

- an individual citizen or resident of the United States;
- a corporation (or any other entity treated as a corporation for U.S. federal income tax purposes) created or organized in or under the laws of the United States, any state thereof or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if it (1) is subject to the primary supervision of a court within the United States and one or more United States persons have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a United States person.

This summary is based upon provisions of the Code and U.S. Treasury regulations, administrative rulings and judicial decisions as of the date hereof. Those authorities may be changed, perhaps retroactively, so as to result in U.S. federal income tax consequences different from those summarized below. We have not sought, and will not seek, any ruling from the United States Internal Revenue Service (the "IRS") with respect to the tax consequences discussed herein, and there can be no assurance that the IRS will not take a position contrary to the tax consequences discussed below or that any position taken by the IRS would not be sustained. This summary does not address all aspects of U.S. federal income taxes, such as the Medicare contribution tax on net investment income, and does not deal with foreign, state, local or other tax considerations that may be relevant to non-U.S. holders in light of their particular circumstances. In addition, it does not describe the U.S. federal income tax consequences applicable to you if you are subject to special treatment under the U.S. federal income tax laws (including if you are a U.S. expatriate, "controlled foreign corporation," "passive foreign investment company," a person who holds or receives our common stock pursuant to the exercise of an employee stock option or otherwise as compensation, a bank, financial institution or other financial services entity, a foreign government or governmental entity, a broker or dealer in foreign currencies, an insurance company, tax-exempt organization, pension plan, real estate investment trust, corporation that accumulates earnings to avoid U.S. federal income tax, person who use or are required to use mark-to-market accounting, person that holds our shares as part of a "straddle," a "hedge," a "conversion transaction," "synthetic security," integrated investment or other risk reduction strategy, or a partnership or other pass-through entity for U.S. federal income tax purposes). We cannot assure you that a change in law will not alter significantly the tax considerations that we describe in this summary.

If a partnership (or any entity treated as such for U.S. federal income tax purposes) holds our common stock, the tax treatment of a partner generally will depend upon the status of the partner and the activities of the partnership. If you are a partner of a partnership (or any entity treated as such for U.S. federal income tax purposes) holding our common stock, you should consult your tax advisors regarding the tax consequences of the purchase, ownership or disposition of our common stock.

If you are considering the purchase of our common stock, you should consult your own tax advisors concerning the particular U.S. federal income tax consequences to you of the purchase, ownership or

disposition of our common stock, as well as the consequences to you arising under the laws of any other taxing jurisdiction.

Dividends

Distributions on our common stock will constitute dividends for U.S. federal income tax purposes to the extent paid out of our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and will first be applied against and reduce a holder's adjusted tax basis in the common stock, but not below zero. Any remaining excess will be treated as capital gain subject to the rules discussed under "Gain on Disposition of Common Stock."

Dividends paid to a non-U.S. holder of our common stock generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. However, dividends that are effectively connected with the conduct of a trade or business by the non-U.S. holder within the United States (and, if required by an applicable income tax treaty, that are attributable to a U.S. permanent establishment of the non-U.S. holder) are not subject to withholding, provided certain certification and disclosure requirements are satisfied, including providing us and/or our paying agent with a validly executed IRS Form W-8ECI. Instead, such dividends are subject to U.S. federal income tax on a net income basis in the same manner as if the non-U.S. holder were a "United States person" as defined under the Code. Any such effectively connected dividends received by a foreign corporation may be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty.

A non-U.S. holder of our common stock who wishes to claim the benefit of an applicable income tax treaty rate and avoid backup withholding, as discussed below, for dividends will be required (a) to complete the applicable IRS Form W-8 certifying under penalty of perjury that such holder is not a United States person and is eligible for treaty benefits or (b) if our common stock is held through certain foreign intermediaries, to satisfy the relevant certification requirements of applicable U.S. Treasury regulations.

A non-U.S. holder of our common stock eligible for a reduced rate of U.S. withholding tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS.

Gain on Disposition of Common Stock

Subject to the discussion of backup withholding and FATCA below, any gain realized on the disposition of our common stock generally will not be subject to U.S. federal income tax unless:

- the gain is effectively connected with a trade or business of the non-U.S. holder in the United States (and, if required by an applicable income tax treaty, is attributable to a United States permanent establishment of the non-U.S. holder);
- the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of that disposition, and certain other conditions are met; or
- we are or have been a "U.S. real property holding corporation," or USRPHC, for U.S. federal income tax purposes at any time within the shorter of the five-year period preceding such disposition or the holder's holding period in the common stock.

A non-U.S. holder described in the first bullet point immediately above will be subject to tax on the net gain derived from the sale under regular graduated U.S. federal income tax rates applicable to such holder as if it were a United States person. In addition, if a non-U.S. holder described in the first bullet point immediately above is a corporation for U.S. federal income tax purposes, it may be subject to the branch profits tax equal to 30% of its effectively connected earnings and profits or at such lower rate as may be specified by an applicable income tax treaty.

An individual non-U.S. holder described in the second bullet point immediately above will be subject to a flat 30% tax on the gain derived from the sale, which may be offset by U.S. source capital losses, even though the individual is not considered a resident of the United States, provided such non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses.

For purposes of the third bullet point immediately above, a corporation generally is a USRPHC if the fair market value of its United States real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. We believe we are not and do not anticipate becoming a USRPHC for U.S. federal income tax purposes. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we became a USRPHC, a non-U.S. holder would not be subject to U.S. federal income tax on a sale, exchange or other taxable disposition of our common stock by reason of our status as a USRPHC so long as our common stock is regularly traded on an established securities market (within the meaning of the applicable regulations) and such non-U.S. holder does not own and is not deemed to own (directly, indirectly or constructively) more than 5% of our outstanding common stock at any time during the shorter of the five year period ending on the date of disposition and such holder's holding period. However, no assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Information Reporting and Backup Withholding

We must report annually to the IRS and to each non-U.S. holder the amount of dividends paid to such holder and the tax withheld with respect to such dividends, regardless of whether withholding was required. Copies of the information returns reporting such dividends and withholding may also be made available to the tax authorities in the country in which the non-U.S. holder resides under the provisions of an applicable income tax treaty.

A non-U.S. holder will be subject to backup withholding for dividends paid to such holder unless such holder certifies under penalty of perjury that it is a non-U.S. holder (and the payor does not have actual knowledge or reason to know that such holder is a United States person as defined under the Code), or such holder otherwise establishes an exemption.

Information reporting and, depending on the circumstances, backup withholding will apply to the proceeds of a sale of our common stock within the United States or conducted through certain U.S.-related financial intermediaries, unless the beneficial owner certifies under penalty of perjury on an applicable IRS Form W-8 that it is a non-U.S. holder (and the payor does not have actual knowledge or reason to know that the beneficial owner is a United States person as defined under the Code), or such owner otherwise establishes an exemption.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a non-U.S. holder's U.S. federal income tax liability provided the required information is timely furnished to the IRS.

Additional Withholding Requirements

Under Sections 1471 through 1474 of the Code (such Sections commonly referred to as "FATCA"), a 30% U.S. federal withholding tax may apply to any dividends paid on our common stock, and, for a disposition of our common stock occurring after December 31, 2018, the gross proceeds from such disposition, in each case paid to (i) a "foreign financial institution" (as specifically defined in the Code) that does not provide sufficient documentation, typically on IRS Form W-8BEN-E, evidencing either (x) an exemption from FATCA or (y) its compliance (or deemed compliance) with FATCA (which may alternatively be in the form of compliance with an intergovernmental agreement with the United States) in a manner that avoids

withholding, or (ii) a "non-financial foreign entity" (as specifically defined in the Code) that does not provide sufficient documentation, typically on IRS Form W-8BEN-E, evidencing either (x) an exemption from FATCA or (y) adequate information regarding certain substantial U.S. beneficial owners of such entity (if any). If a dividend payment is both subject to withholding under FATCA and subject to the withholding tax discussed above under "Dividends," the withholding under FATCA may be credited against, and therefore reduce, such other withholding tax. You should consult your own tax advisor regarding these requirements and whether they may be relevant to your ownership and disposition of our common stock

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is not complete and may not contain all the information you should consider before investing in our capital stock. This description is summarized from, and qualified in its entirety by reference to, our Amended and Restated Articles of Incorporation ("Articles") and our Bylaws ("Bylaws"), in each case as amended to the date of this prospectus supplement, which have been publicly filed with the SEC. See "Where You Can Find More Information; Incorporation of Certain Information by Reference." In addition, please refer to our other publicly filed documents incorporated herein by reference which describe our outstanding registration rights, equity incentive plans and other securities.

COMMON STOCK

Under our Articles, we are authorized to issue up to 50,000,000 shares of common stock, par value $0.01 per share. As of March 31, 2018, 34,669,276 shares of common stock were outstanding.

Dividends, Voting Rights and Liquidation

The holders of shares of our common stock: (i) have equal, ratable rights to dividends from funds legally available therefor, when, as and if declared by the Board of Directors, (ii) are entitled to share ratably in all assets available for distribution to holders of shares of common stock upon liquidation, dissolution or winding up of our affairs, (iii) do not have preemptive, subscription or conversion rights and there are no redemption or sinking fund provisions applicable thereto and (iv) are entitled to one vote per share on all matters which shareholders may vote on at all meetings of shareholders. Except as otherwise required by statute, our Articles or our Bylaws, all matters are decided by a majority vote of the number of shares entitled to vote at the time of the vote.

Transfer Agent and Registrar

Broadridge Corporate Issuer Solutions, Inc. is the transfer agent and registrar for our common stock.

Minnesota Anti-Takeover Laws

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 common stock at a premium over the market price.

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 stock, 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.

Registration Rights

In connection with that certain Securities Purchase Agreement, dated as of August 26, 2015, between us and EW Healthcare Partners L.P., formerly named Essex Woodlands Fund IX, L.P. ("Essex"), we entered into a Registration Rights Agreement with Essex, pursuant to which we granted Essex certain demand and "piggy-back" registration rights with respect to its shares of our common stock. The resale of all of Essex's shares has been registered pursuant to the Registration Rights Agreement.

WHERE YOU CAN FIND MORE INFORMATION;

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

We file annual, quarterly and current reports, proxy statements and other documents with the SEC, under the Exchange Act. You may read and copy any materials that we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Our reports, proxy statements and other documents filed electronically with the SEC are available at the website maintained by the SEC at http://www.sec.gov. You can read and copy reports and other information concerning us at the offices of the Financial Industry Regulatory Authority, located at 1735 K Street, Washington D.C. 20006. We also make available free of charge on or through our Internet website, http://www.axogeninc.com, our annual, quarterly and current reports, and, if applicable, amendments to those reports, filed or furnished pursuant to Section 13(a) of the Exchange Act, as soon as reasonably practicable after we electronically file such reports with the SEC. Information on our website is not a part of this prospectus supplement or the accompanying prospectus.

The SEC allows us to "incorporate by reference" in this prospectus supplement information that we file with the SEC, which means we can disclose important information to you by referring you to other documents that contain that information. The information we incorporate by reference is considered to be part of this prospectus supplement and information we later file with the SEC will automatically update and supersede the information in this prospectus supplement. The following documents filed by us with the SEC pursuant to Section 13 of the Exchange Act (File No. 001-36046) and any future filings under Sections 13(a), 13(c), 14 or 15 (d) of the Exchange Act, except for information furnished under Item 2.02 or 7.01 of Current Report on Form 8-K, or exhibits related thereto, made after the date of the initial registration statement and prior to effectiveness of the registration statement and before the termination of the offering are incorporated by reference herein:

- our annual report on Form 10-K for the fiscal year ended December 31, 2017, filed with the SEC on February 28, 2018;
- the information specifically incorporated by reference into our annual report from our definitive proxy statement on Schedule 14A, filed with the SEC on March 29, 2018, as amended and supplemented by the Definitive Additional Materials on Schedule 14A that we filed with the SEC on March 29, 2018 and March 30, 2018;
- our quarterly report on Form 10-Q for the quarter ended March 31, 2018, filed with the SEC on April 30, 2018;
- our current reports on Form 8 K, filed with the SEC on January 5, 2018, March 13, 2018 and April 13, 2018; and
- the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on August 6, 2013, including any amendment or report filed for the purpose of updating such description.

Any statement contained in this prospectus supplement, the accompanying prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus supplement or the accompanying prospectus will be deemed to be modified or superseded to the extent that a statement contained in this prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You may request, orally or in writing, a copy of these documents, which will be provided to you at no cost, by contacting: Investor Relations, c/o AxoGen, Inc., 13631 Progress Boulevard, Suite 400, Alachua, Florida 32615. Our telephone number is (386) 462-6800.

LEGAL MATTERS

Legal matters with respect to the securities offered hereby are being passed upon for us by DLA Piper LLP (US). Certain legal matters will be passed upon on behalf of the underwriters by Latham & Watkins LLP.

EXPERTS

The consolidated financial statements and schedule of AxoGen, Inc. and its subsidiaries as of December 31, 2017 and 2016, and the related consolidated statements of operations, shareholders' equity and cash flows for each of the years in the three-year period ended December 31, 2017, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2017, have been incorporated by reference herein in reliance upon the reports of Lurie, 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

PROSPECTUS

Common Stock

We may from time to time offer to sell common stock in amounts, at prices and on terms described in one or more supplements to this prospectus. This prospectus provides a general description of our common stock. Each time we sell shares of our common stock, we will provide the specific terms of the shares in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with such offerings. The prospectus supplement and any related free writing prospectus may 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 the documents incorporated by reference herein and therein, before you invest in any of our common stock.

We may offer and sell our common stock through underwriters, dealers or agents, or directly to purchasers, or through a combination of these methods. See "Plan of Distribution" beginning on page 10 of this prospectus.

Our common stock is listed on the Nasdaq Capital Market under the symbol "AXGN." The last reported sale price of our common stock on the Nasdaq Capital Market on May 4, 2018 was $42.50 per share.

Investing in our securities involves risk. See "Risk Factors" on page 5 of this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as the documents incorporated by reference herein and therein, before you invest in any of our securities.

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

The date of this prospectus is May 7, 2018

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the U.S. Securities and Exchange Commission (the "SEC") using a "shelf" registration process as a "well-known seasoned issuer," as defined in Rule 405 under the Securities Act of 1933, as amended (the "Securities Act"). Under this shelf registration process, we may offer and sell, from time to time, in one or more offerings the common stock described in this prospectus.

This prospectus provides you with a general description of the securities we may offer. Each time we sell the securities, we will, to the extent required by law, provide a prospectus supplement that will contain specific information about the terms of the offering. We may also authorize one or more free writing prospectuses to be provided to you in connection with the offering. The prospectus supplement and any related free writing prospectus may add, update or change information contained in this prospectus. This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits. You should carefully read this prospectus, the applicable prospectus supplement, and any applicable free writing prospectus, as well as the information and documents incorporated herein and therein by reference and the additional information under the heading "Where You Can Find More Information," before making an investment decision.

We have not authorized any dealer, salesman or other person to give any information or to make any representation other than those contained in, or incorporated by reference into, this prospectus and the applicable prospectus supplement, and any free writing prospectus we have authorized for use in connection with a specific offering. You must not rely upon any other information or representation.

This prospectus and any accompanying supplement to this prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and any accompanying supplement to this prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus, any accompanying prospectus supplement and any applicable free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus, any accompanying prospectus supplement or any applicable free writing prospectus is delivered, or securities sold, on a later date.

This prospectus may not be used by us to consummate sales of our securities unless it is accompanied by a prospectus supplement. To the extent there are inconsistencies between any prospectus supplement, this prospectus and any documents incorporated by reference, the document with the most recent date will control.

Unless the context otherwise requires, references in this prospectus to "we," "us," "our," or the "Company" refer to AxoGen, Inc. and its wholly owned subsidiaries, AxoGen Corporation and AxoGen Europe GmbH.

This prospectus includes trademarks, tradenames and service marks that are the property of us and of other organizations. Solely for convenience, trademarks, trade names and service marks referred to in this prospectus may appear without the "™," "®," "©" or "SM" symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks, trade names and service marks. We do not intend our use or display of other parties' trademarks, trade names or service marks to imply, and such use or display should not be construed to imply, a relationship with, or endorsement or sponsorship of us by, these other parties.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus or incorporated by reference into this prospectus. This summary does not contain all the information that you should consider before investing in our securities. You should carefully read this entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including each of the documents incorporated herein or therein by reference, before making an investment decision.

Overview

We are a global leader in developing and marketing surgical solutions for peripheral nerves. We provide products and education to improve surgical treatment algorithms for peripheral nerve damage or discontinuity. Our portfolio of products includes Avance Nerve Graft, an off-the-shelf processed human nerve allograft for bridging severed peripheral nerves without the comorbidities associated with a second surgical site, AxoGuard Nerve Connector, a porcine submucosa extracellular matrix ("ECM") coaptation aid for tensionless repair of severed peripheral nerves, AxoGuard Nerve Protector, a porcine submucosa ECM product used to wrap and protect damaged peripheral nerves and reinforce the nerve reconstruction while preventing soft tissue attachments, and Avive Soft Tissue Membrane, a minimally processed human umbilical cord membrane that may be used as a resorbable soft tissue covering to separate tissues and modulate inflammation in the surgical bed. Along with these core surgical products, we also offer the AxoTouch Two-Point Discriminator and AcroVal Neurosensory and Motor Testing System. These evaluation and measurement tools assist healthcare professionals in detecting changes in sensation, assessing return of sensory, grip and pinch function, evaluating effective treatment interventions, and providing feedback to patients on peripheral nerve function. Our portfolio of products is available in the United States, Canada, the United Kingdom and several European and other international countries.

We began marketing products in 2008 and our revenues have increased from approximately $4.8 million in 2011 to approximately $60.4 million in 2017. Gross profit for the year ended December 31, 2017 was approximately $51.1 million, while our loss from operations for the year ended December 31, 2017 was approximately $8.0 million. We have continued to broaden our sales and marketing focus, which we expect to have a continuing positive contribution to our revenue growth in the long term.

Avance Nerve Graft and Avive Soft Tissue Membrane are processed in the United States at our processing facility in Dayton, Ohio. AxoGuard Nerve Connector and AxoGuard Nerve Protector are manufactured in the United States by Cook Biotech Incorporated and are exclusively distributed by us worldwide. The AcroVal Neurosensory and Motor Testing System and AxoTouch Two Point Discriminator are contract manufactured by Viron Technologies, LLC (formerly Cybernetics Research Laboratories) ("Viron") in Tucson, Arizona. Viron supplies the AcroVal Neurosensory and Motor Testing System and AxoTouch Two Point Discriminator unpackaged and they are packaged at our distribution facility in Burleson, Texas.

Peripheral Nerve Regeneration Market Overview

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

Every day patients suffer traumatic bodily injuries resulting in damage or discontinuity to peripheral nerves severe enough to require surgical treatment, including injuries from motor vehicle

accidents, power tool injuries, gunshot wounds, dislocations, fractures, lacerations, or other forms of penetrating trauma. The peripheral nerves commonly damaged or discontinued from these traumas include the digital, median, ulnar, radial, facial, spinal accessory and brachial plexus nerves. The "Extremity Trauma" portion of the Market (as defined below) encompasses the traumatic PND described above but excludes the OMF, Breast and Carpal Tunnel (as such terms are defined below) portions of the Market.

Beyond the physical damage or discontinuity to peripheral nerves resulting from traumatic bodily injury described above, peripheral nerve damage or discontinuity also occurs due to surgical intervention. Nerve damage or discontinuity can occur during dental and oral surgery procedures such as third molar extractions, placement of dental implants and removal of tumors during which one or more sections of the trigeminal nerve can be damaged or discontinued ("OMF"). This can result in numbness in certain areas of the face and mouth.

Breast reconstruction neurotization ("Breast") is another portion of the Market. Currently, when a woman undergoes autologous breast reconstruction after a mastectomy, she receives the shape of a natural breast but loses sensory feeling. This forfeiture of sensation can have a profound effect contributing to quality of life issues such as depression and other emotional challenges. In certain cases, sensation can be returned to the breast area with the use of the Company's products through an innovative surgical technique called ReSensation. The Company believes that the ideal breast reconstruction should restore size, shape, symmetry, softness and now, sensation—without the potential risks and co-morbidity associated with autograft. The ReSensation technique incorporates the Company's vision into a reproducible and efficient solution for reconstructive plastic surgeons.

Finally, peripheral nerves can also be damaged due to compression injuries. For instance, severe and recurrent carpal tunnel cases may result in complications and damage to the peripheral nerve that requires surgical intervention and protection of the peripheral nerve. PND caused by recurrent carpal tunnel syndrome and cubital tunnel syndrome constitutes the "Carpal Tunnel" portion of the Market.

We estimate the United States PND market for our current product portfolio for Extremity Trauma, OMF, Breast and Carpal Tunnel is $2.2 billion (the "Market"). From a product prospective, as to the Market, we estimate that Avance Nerve Graft represents $976 million, AxoGuard Nerve Connector represents $391 million, AxoGuard Nerve Protector represents $433 million and Avive Soft Tissue Membrane represents $439 million.

We estimate that the Extremity Trauma portion of the Market is approximately $1.5 billion. The estimated size of the Extremity Trauma portion of the market is based upon epidemiological studies regarding the general number of trauma patients, physician interviews and incidence of PND in the population. We believe that each year in the U.S., more than 1.4 million people suffer damage or discontinuity to peripheral nerves resulting in over 700,000 extremity nerve repair procedures.

We estimate that the OMF portion of the Market is approximately $293 million, based upon research that has indicated approximately 80,350 PND occur in the U.S. each year that are related to benign tumor resections, third molar surgeries, anesthetic injections and dental implants. We have applied the average sales price of the Avance Nerve Graft, AxoGuard Nerve Connector and AxoGuard Nerve Protector that address such PND in order to derive the OMF portion of the Market.

According to market data, there are annually 307,660 breast cancer patients of which 113,834 receive a mastectomy. Of those mastectomy patients, every year, more than 20,000 women choose autologous flap reconstruction as compared to implant based reconstructions. Removing those procedures that are not appropriate for neurotization, and based upon our assumption that 65% of women will elect to have a bilateral procedure, we estimate that the Breast portion of the Market is approximately $250 million.

We estimate that the Carpal Tunnel portion of the Market is approximately $188 million, or 118,000 procedures. According to literature, there are approximately 500,000 primary carpal tunnel and 53,000 primary cubital tunnel relief surgeries performed annually in the U.S. For carpal tunnel, we estimate that our addressable market is the 20% of carpal tunnel surgeries that require revision procedures to address the recurrence of symptoms. From the 53,000 primary cubital tunnel surgeries, we estimate that our addressable market is 18,000 of such surgeries comprised of revision and primary interventions. As a result, we estimate that approximately 100,000 carpal tunnel revision surgeries and 18,000 total cubital tunnel procedures are addressable each year in the U.S. to mitigate the recurrence of symptoms. These revision and primary surgeries are required due to compression of the peripheral 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 procedures.

Market Expansion Opportunities

Although distribution and sales of products in the Extremity Trauma, OMF, Breast and Carpal Tunnel portions of the Market constitute our prime revenue sources today, market expansion opportunities in lower extremity surgery, head and neck surgery, urology and the surgical intervention for pain offer us new and expanded revenue opportunities. For example, we have developed the AxoGuard NerveCap which is designed to protect a peripheral nerve end and separate the nerve from the surrounding environment to reduce the development of asymptomatic or painful neuromas ("Neuroma Management"). A neuroma is a tangled mass of disorganized nerve and fibrous tissue which, if not properly diagnosed and addressed, can require long term pharmacologic treatment and pain management. An example of the use of the AxoGuard Nerve Cap is in the situation of a digital amputation whereby the nerves that are cut in the amputation may form a neuroma if the nerve end is not properly terminated or capped. In 2018, we intend to conduct clinical evaluation and user preference studies of the AxoGuard Nerve Cap and define our marketing plan for Neuroma Management.

Lower limb/total join replacement is another market opportunity. In the United States there are approximately 700,000 total knee replacements ("TKR") per year and 310,000 total hip replacements ("THR") per year. We estimate that 6% of patients have neuropathic pain with TKR and THR and more than 60,000 have neuropathic pain post joint replacement. We believe if we proceed with entering this area in the future it would increase the market for our products by approximately $125 million.

Corporate Information

We were incorporated in Minnesota in 1977. Our principal offices are located at 13631 Progress Boulevard, Suite 400, Alachua, Florida 32615. Our telephone number is (386) 462-6800. We have two wholly owned subsidiaries, AxoGen Corporation, a Delaware corporation, and AxoGen Europe GmbH, a limited liability corporation with its corporate seat in Vienna, Austria. Our web address is *www.axogeninc.com*. Information contained in, or accessible through, our website does not constitute a part of this prospectus or any accompanying prospectus supplement.

Our reports that have been filed with the SEC are available on our website free of charge, including our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, Forms 3, 4 and 5 filed on behalf of directors and executive officers and any amendments to such reports filed pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Copies of this prospectus and the applicable prospectus supplement may also be obtained without charge electronically or by paper by contacting Investor Relations, c/o AxoGen, Inc., 13631 Progress Boulevard, Suite 400, Alachua, Florida 32615 or by calling (386) 462-6800.

RISK FACTORS

An investment in our common stock involves risks. Prior to making a decision about investing in our common stock, you should carefully consider the specific risks discussed under "Risk Factors" in our annual report on Form 10-K for our most recent fiscal year, as updated by our quarterly reports on Form 10-Q and other SEC filings subsequent thereto, pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, and in any applicable prospectus supplement. The risks and uncertainties described in any applicable prospectus supplement and in our SEC filings are not the only ones facing us. Each of these risks could materially and adversely affect our business, results of operations and financial condition, resulting in a decline in the trading price of our common stock and a complete or partial loss of your investment.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, any accompanying prospectus supplement or related free writing prospectus, and the documents incorporated by reference herein and therein may contain "forward-looking statements" within the meaning of the safe harbor provisions of Section 27A of the Securities Act, Section 21E of the Exchange Act, and the Private Securities Litigation Reform Act of 1995. These forward-looking statements only provide our current expectations or forecasts of future events and financial performance and may be identified by the use of forward-looking terminology, including the terms "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "will," "should," "could," "predicts," or the negative thereof, or other variations or comparable terminology, though the absence of these words does not necessarily mean that a statement is not forward-looking. Forward-looking statements include all matters that are not historical facts and include, without limitation, statements concerning our business strategy, outlook, objectives, future milestones, plans, intentions, goals, and future financial condition, including the period of time for which our existing resources will enable us to fund our operations.

You should read carefully the risks described in the section entitled "Risk Factors" beginning on page 5 of this prospectus, and in any accompanying prospectus supplement or related free writing prospectus, together with all information incorporated by reference herein and therein, to better understand the significant risks and uncertainties inherent in our business and underlying any forward-looking statements. As a result of these risks, actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements in this prospectus or in any accompanying prospectus supplement or related free writing prospectus, or incorporated by reference herein and therein, and you should not place undue reliance on any forward-looking statements.

Any forward-looking statements that we make in this prospectus speak only as of the date of such statements and we undertake no obligation to publicly update any forward-looking statements or to publicly announce revisions to any of the forward-looking statements, whether as a result of new information, future events or otherwise.

DESCRIPTION OF THE SECURITIES WE MAY OFFER

The following description of our capital stock is not complete and may not contain all the information you should consider before investing in our capital stock. This description is summarized from, and qualified in its entirety by reference to, our Amended and Restated Articles of Incorporation ("Articles") and our Bylaws ("Bylaws"), in each case as amended to the date of this prospectus, which have been publicly filed with the SEC. See "Where You Can Find More Information" and "Incorporation of Certain Information by Reference." In addition, please refer to our other publicly filed documents incorporated herein by reference which describe our outstanding registration rights, equity incentive plans and other securities.

COMMON STOCK

Under our Articles, we are authorized to issue up to 50,000,000 shares of common stock, par value $0.01 per share. As of May 4, 2018, 34,697,845 shares of common stock were issued and outstanding.

Dividends, Voting Rights and Liquidation

The holders of shares of our common stock: (i) have equal, ratable rights to dividends from funds legally available therefor, when, as and if declared by the Board of Directors, (ii) are entitled to share ratably in all assets available for distribution to holders of shares of common stock upon liquidation, dissolution or winding up of our affairs, (iii) do not have preemptive, subscription or conversion rights and there are no redemption or sinking fund provisions applicable thereto and (iv) are entitled to one vote per share on all matters which shareholders may vote on at all meetings of shareholders. Except as otherwise required by statute, our Articles or our Bylaws, all matters are decided by a majority vote of the number of shares entitled to vote at the time of the vote.

Transfer Agent and Registrar

Broadridge Corporate Issuer Solutions, Inc. is the transfer agent and registrar for our common stock.

Minnesota Anti-Takeover Laws

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

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 stock, 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.

Registration Rights

In connection with that certain Securities Purchase Agreement, dated as of August 26, 2015, between us and EW Healthcare Partners L.P., formerly named Essex Woodlands Fund IX, L.P. ("Essex"), we also entered into a Registration Rights Agreement with Essex, pursuant to which we granted Essex certain demand and "piggy-back" registration rights with respect to its shares of our common stock. The resale of all of Essex's shares has been registered pursuant to the Registration Rights Agreement.

USE OF PROCEEDS

Unless the applicable prospectus supplement states otherwise, we anticipate that the net proceeds from the sale of our securities will be used for general corporate purposes, and we will retain broad discretion with respect to the allocation thereof.

PLAN OF DISTRIBUTION

We may offer securities under this prospectus from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or dealers, through agents and/or directly to one or more purchasers. The securities may be distributed 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;
- at negotiated prices; or
- a combination of these pricing methods.

We may also sell equity securities covered by this registration statement in an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price on or through the facilities of Nasdaq or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale.

Such at the market offerings, if any, may be conducted by underwriters acting as principal or agent.

Each time that securities covered by this prospectus are sold, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms and conditions of the offering of such securities, including the offering price of the securities and the proceeds to us, if applicable.

Offers to purchase the securities being offered by this prospectus may be solicited directly. Agents may also be designated to solicit offers to purchase the securities from time to time. Any agent involved in the offer or sale of our securities will be identified in a prospectus supplement.

If a dealer is utilized in the sale of the securities being offered by this prospectus, the securities will be sold to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If an underwriter is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the underwriter at the time of sale and the name of any underwriter will be provided in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we, or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for which they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the securities at varying prices to be determined by the dealer.

Any compensation paid to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers will be provided in the applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We

may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof and to reimburse those persons for certain expenses.

To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

If indicated in the applicable prospectus supplement, underwriters or other persons acting as agents may be authorized to solicit offers by institutions or other suitable purchasers to purchase the securities at the public offering price set forth in the prospectus supplement, pursuant to delayed delivery contracts providing for payment and delivery on the date or dates stated in the prospectus supplement. These purchasers may include, among others, commercial and savings banks, insurance companies, pension funds, investment companies and educational and charitable institutions. Delayed delivery contracts will be subject to the condition that the purchase of the securities covered by the delayed delivery contracts will not at the time of delivery be prohibited under the laws of any jurisdiction in the United States to which the purchaser is subject. The underwriters and agents will not have any responsibility with respect to the validity or performance of these contracts.

We may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

In compliance with the guidelines of the Financial Industry Regulatory Authority, Inc. ("FINRA"), the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate proceeds of the offering.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

General Information

Underwriters, dealers and agents that participate in the distribution of our securities may be underwriters as defined in the Securities Act, and any discounts or commissions they receive and any profit they make on the resale of the offered securities may be treated as underwriting discounts and commissions under the Securities Act. Any underwriters or agents will be identified and their compensation described in a prospectus supplement. We may indemnify agents, underwriters, and dealers against certain civil liabilities, including liabilities under the Securities Act, or make contributions to payments they may be required to make relating to those liabilities. Our agents, underwriters, and dealers, or their affiliates, may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

Representatives of the underwriters through whom our securities are sold for public offering and sale may engage in over-allotment, stabilizing transactions, syndicate short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves syndicate sales in excess of the offering size, which creates a syndicate short position. Stabilizing transactions permit bids to purchase the offered securities so long as the stabilizing bids do not exceed a specified maximum.

Syndicate covering transactions involve purchases of the offered securities in the open market after the distribution has been completed in order to cover syndicate short positions. Penalty bids permit the representative of the underwriters to reclaim a selling concession from a syndicate member when the offered securities originally sold by such syndicate member are purchased in a syndicate covering transaction to cover syndicate short positions. Such stabilizing transactions, syndicate covering transactions and penalty bids may cause the price of the offered securities to be higher than it would otherwise be in the absence of such transactions. These transactions may be effected on a national securities exchange and, if commenced, may be discontinued at any time.

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

We will bear all costs, expenses and fees in connection with the registration of the securities as well as the expense of all commissions and discounts, if any, attributable to the sales of any of our securities by us.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy any document we file with the SEC at the SEC's public reference room at 100 F Street, N.E., Washington, D.C. 20549 on official business days during the hours of 10:00am and 3:00pm. Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. The SEC maintains a website at http://www.sec.gov that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. In addition, we maintain a website at http://www.axogeninc.com and make available free of charge on this website our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information contained in, or accessible through, our website does not constitute a part of this prospectus or any accompanying prospectus supplement.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" much of the information we file with it, which means that we can disclose important information to you by referring you to those publicly available documents. All of the information that we incorporate by reference is considered to be part of this prospectus, and any of our subsequent filings with the SEC will automatically update and supersede this information. This prospectus incorporates by reference the documents listed below and any future filings made by AxoGen with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, except for information furnished under Items 2.02 or 7.01 of our current reports on Form 8-K, or exhibits related thereto, between the date of this prospectus and the termination of the offering of the securities:

- our annual report on Form 10-K for the fiscal year ended December 31, 2017, filed with the SEC on February 28, 2018;
- the information specifically incorporated by reference into our annual report from our definitive proxy statement on Schedule 14A, filed with the SEC on March 29, 2018, as amended and supplemented by the Definitive Additional Materials on Schedule 14A that we filed with the SEC on March 29, 2018 and March 30, 2018;
- our quarterly report on Form 10-Q for the quarter ended March 31, 2018, filed with the SEC on April 30, 2018;
- our current reports on Form 8-K, filed with the SEC on January 5, 2018, March 13, 2018, and April 13, 2018; and
- the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on August 6, 2013, including any amendment or report filed for the purpose of updating such description.

Any statement contained in any document incorporated by reference herein will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any additional prospectus supplements modifies or supersedes such statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

We will provide, upon written or oral request, at no cost, to each person, including any beneficial owner, to whom a prospectus is delivered, a copy of any or all of the information that has been incorporated by reference in the prospectus but not delivered with the prospectus. You may request a

copy of these filings by writing us at Investor Relations, c/o AxoGen, Inc., 13631 Progress Boulevard, Suite 400, Alachua, Florida 32615. Our telephone number is (386) 462-6800.

You should rely only on the information incorporated by reference or provided in this prospectus or any supplement. We have not authorized anyone else to provide you with different information. You should not assume that information in this prospectus or any supplement is accurate as of any date other than the date on the front of these documents.

LEGAL MATTERS

Legal matters with respect to the securities offered hereby are being passed upon for us by DLA Piper LLP (US), Short Hills, New Jersey.

EXPERTS

The consolidated financial statements and schedule of AxoGen, Inc. and its subsidiaries as of December 31, 2017 and 2016, and the related consolidated statements of operations, shareholders' equity and cash flows for each of the years in the three-year period ended December 31, 2017, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2017, have been incorporated by reference herein in reliance upon the reports of Lurie, 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

3,000,000 Shares

AxoGen, Inc.

Common Stock

PROSPECTUS

Joint Book-Running Managers

Jefferies

Leerink Partners

Co-Managers

William Blair

JMP Securities

May 8, 2018