

AGENUS INC
Form 424B5
May 20, 2015
Table of Contents

Filed pursuant to Rule 424(b)5
Registration No. 333-199255

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been filed with the Securities and Exchange Commission and is effective. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and they are not soliciting an offer to buy these securities in any state or other jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MAY 20, 2015

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus dated October 23, 2014)

Shares

Agenus Inc.

Common Stock

We are offering _____ shares of our common stock, par value \$0.01 per share. Our common stock is traded on the Nasdaq Capital Market under the symbol AGEN. On May 19, 2015, the last reported sale price of our common stock on the Nasdaq Capital Market was \$6.69 per share.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page S-5 of this prospectus supplement and page 4 of the accompanying prospectus and the documents incorporated by reference in this prospectus supplement.

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

	PER SHARE	TOTAL
Public offering price	\$	\$
Underwriting discounts and commissions	\$	\$
Proceeds to Agenus (before expenses)	\$	\$

Delivery of the shares of common stock is expected to be made on or about May , 2015. We have granted the underwriters an option for a period of 30 days to purchase up to an additional shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$ and the total proceeds to us, before expenses, will be \$.

Joint Book-Running Managers

Jefferies

William Blair

Co-Manager

Oppenheimer & Co.

Prospectus Supplement dated May , 2015

Table of Contents

TABLE OF CONTENTS

PROSPECTUS SUPPLEMENT	PAGE
<u>ABOUT THIS PROSPECTUS SUPPLEMENT</u>	S-ii
<u>PROSPECTUS SUPPLEMENT SUMMARY</u>	S-1
<u>CAUTIONARY NOTE ABOUT FORWARD-LOOKING STATEMENTS</u>	S-4
<u>RISK FACTORS</u>	S-5
<u>USE OF PROCEEDS</u>	S-32
<u>DILUTION</u>	S-33
<u>MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSEQUENCES TO NON-U.S. HOLDERS</u>	S-35
<u>UNDERWRITING</u>	S-39
<u>DESCRIPTION OF COMMON STOCK</u>	S-45
<u>LEGAL MATTERS</u>	S-46
<u>EXPERTS</u>	S-47
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	S-48
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	S-49

PROSPECTUS	PAGE
<u>ABOUT THIS PROSPECTUS</u>	1
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	2
<u>CAUTIONARY NOTE ABOUT FORWARD-LOOKING STATEMENTS</u>	3
<u>RISK FACTORS</u>	4

<u>THE COMPANY</u>	5
<u>USE OF PROCEEDS</u>	7
<u>RATIO OF EARNINGS TO FIXED CHARGES</u>	8
<u>DILUTION</u>	9
<u>DESCRIPTION OF SECURITIES</u>	10
<u>DESCRIPTION OF CAPITAL STOCK</u>	11
<u>DESCRIPTION OF COMMON STOCK</u>	12
<u>DESCRIPTION OF PREFERRED STOCK</u>	15
<u>DESCRIPTION OF WARRANTS</u>	17
<u>DESCRIPTION OF DEBT SECURITIES</u>	21
<u>DESCRIPTION OF UNITS</u>	28
<u>LEGAL OWNERSHIP AND BOOK-ENTRY ISSUANCE</u>	32
<u>PLAN OF DISTRIBUTION</u>	36
<u>LEGAL MATTERS</u>	38
<u>EXPERTS</u>	39
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	40

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This document consists of two parts. The first part is this prospectus supplement, which describes the specific terms of this offering. The second part, the accompanying prospectus, gives more general information, some of which may not apply to this offering. Generally, when we refer only to the prospectus, we are referring to both parts combined. This prospectus supplement may add to, update or change information in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement or the accompanying prospectus.

If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement. This prospectus supplement, the accompanying prospectus and the documents incorporated into each by reference include important information about us, the shares being offered and other information you should know before investing in our common stock.

You should rely on this prospectus supplement, the accompanying prospectus and the information incorporated or deemed to be incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not, and the underwriters have not, authorized anyone to provide you with information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We are not, and the underwriters are not, offering to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus is accurate as of any date other than as of the date of this prospectus supplement or the accompanying prospectus, as the case may be, or in the case of the documents incorporated by reference, the date of such documents regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our common stock. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates.

All references in this prospectus supplement or the accompanying prospectus to Agenus, Antigenics, the Company, we, us or our mean Agenus Inc. and its subsidiaries, unless we state otherwise or the context otherwise requires.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

The following is a summary of selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. It does not contain all of the information that you should consider before buying our securities. You should read this prospectus supplement and the accompanying prospectus in their entirety, including the Risk Factors section contained in this prospectus supplement and the accompanying prospectus and our consolidated financial statements and the related notes and the other documents incorporated by reference herein and therein.

Our Business

We are an immunotherapy company discovering and developing innovative treatments for patients with cancer and other diseases in which modulation of immune function could provide therapeutic benefit. Our approaches are driven by three platform technologies:

- n our antibody platforms, including our proprietary Retrocyte Display and SECANT[®] technologies, and our antibody programs, including checkpoint modulators, or CPMs;

- n our heat shock protein (HSP)-based vaccines; and

- n our saponin-based vaccine adjuvants, principally our QS-21 Stimulon[®] adjuvant, or QS-21 Stimulon.

We have a portfolio of programs in pre-clinical and clinical stages, including a series of CPMs in investigational new drug (IND)-enabling studies, a Phase 3 ready HSP-based autologous vaccine for glioblastoma multiforme, or GBM, a form of brain cancer, and a number of advanced QS-21 Stimulon-containing vaccine candidates in late stage development by our partner, GlaxoSmithKline (GSK).

For the treatment of cancer, our programs aim to stimulate the immune system to recognize and eradicate cancer cells and disable the mechanisms that cancer cells employ to evade detection and destruction by the immune system. Because of the breadth of our portfolio, we have the ability to combine our proprietary vaccines with a portfolio of checkpoint modulating antibodies against major checkpoint targets to explore and optimize cancer treatments. Our strategy is to develop these agents either alone or in combinations to yield best-in-class treatments. We assess the development, commercialization and/or partnering strategies with respect to each of our internal product candidates periodically based on several factors, including clinical trial results, competitive positioning and funding requirements and resources.

Our Retrocyte Display platform has been applied to the discovery and development of CPMs targeting significant checkpoint targets. We and our partners currently have pre-clinical programs targeting GITR, OX40, CTLA-4, LAG-3, TIM-3 and PD-1. In April 2015, we expanded our antibody discovery platform through the acquisition of key antibody assets from Celexion, LLC. Among the acquired assets was the SECANT yeast display platform for the generation of novel monoclonal antibodies and efficient integration of drug targets such as CPMs.

In January 2015, we announced a broad, global alliance with Incyte Corporation, or Incyte, to pursue the discovery and development of CPMs that initially target GITR, OX40, TIM-3 and LAG-3, and potentially other antibodies for the treatment of patients with cancer. We also began collaborating with Merck Sharpe & Dohme, or Merck, in April

2014 to discover antibodies against two undisclosed checkpoint targets. We plan to file two INDs in 2015 for CPM antibody candidates targeting GITR and CTLA-4, and we anticipate initiating clinical trials with the first of our CPM antibody candidates in 2016.

In addition to our internal development efforts, we continue to pursue collaborative, out-licensing and/or partnering opportunities for our portfolio programs and product candidates, as well as explore in-licensing, acquisitions and collaborative arrangements in areas of synergy with our existing programs. Our business activities have included product research and development, intellectual property prosecution, manufacturing, regulatory and clinical affairs, corporate finance and development activities, and support of our collaborations.

S-1

Table of Contents

As of March 31, 2015, we had cash and cash equivalents of \$79.3 million. Our current cash balance, together with the anticipated proceeds of this offering, is expected to satisfy our liquidity requirements into 2017. Subject to market and other conditions, we may seek additional funding through public or private financings of equity or debt securities, but such financing may not be available on acceptable terms, or at all. In addition, the terms of such financings may result in, among other things, dilution for stockholders or the incurrence of indebtedness that may impact our ability to make capital expenditures or incur additional debt. We may also seek additional funds through arrangements with collaborators or other third parties, or through project financing. For example, we are currently exploring options to advance our Prophage vaccine candidate into a Phase 3 clinical trial for newly diagnosed GBM, as well as the possibility of monetizing all or part of the potential royalties we are entitled to receive from our QS-21 partners. Any of the foregoing arrangements would generally require us to relinquish or encumber rights to some of our technologies or product candidates, and we may not be able to enter into such arrangements on acceptable terms, if at all. If we are unable to obtain additional funding on a timely basis, we may be required to curtail or terminate some or all of our product development programs or to scale back, suspend or terminate our business operations.

Risk Factors

Our business is subject to substantial risk. Please carefully consider the **Risk Factors** beginning on page S-5 of this prospectus supplement and page 4 of the accompanying prospectus and other information included and incorporated by reference in this prospectus supplement and the accompanying prospectus, including the risk factors incorporated by reference from our filings with the Securities and Exchange Commission, or the SEC, for a discussion of the factors you should consider carefully before deciding to purchase these securities. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. You should be able to bear a complete loss of your investment.

Corporate Information

Our principal executive office is located at 3 Forbes Road, Lexington, MA, 02421, and our telephone number is (781) 674-4400. Our Internet website address is www.agenusbio.com. **The contents of our website are not part of, or incorporated into, this prospectus supplement or the accompanying prospectus.**

Table of Contents

THE OFFERING

*The following summary contains basic information about our common stock and the offering and is not intended to be complete. It does not contain all the information that may be important to you. For a more complete understanding of our common stock, you should read the sections entitled *Description of Common Stock* in this prospectus supplement and the accompanying prospectus.*

Common stock offered by us	shares
Common stock to be outstanding immediately after the offering	shares (or shares if the underwriters exercise in full their option to purchase additional shares)
Option to purchase additional shares	We have granted the underwriters an option to purchase up to additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.
Use of proceeds	We intend to use the net proceeds from this offering to fund our continued research and development initiatives in connection with expanding our product pipeline and for other general corporate purposes, which may include working capital, capital expenditures, clinical trial expenditures, acquisitions of additional companies or technologies and investments. See Use of Proceeds.
Risk factors	Investing in our common stock involves a high degree of risk. You should consider the Risk Factors beginning on page S-5 of this prospectus supplement and page 4 of the accompanying prospectus and incorporated by reference in this prospectus supplement and the accompanying prospectus, including the risk factors incorporated by reference from our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2015, before buying shares of our common stock.
Nasdaq Capital Market symbol	AGEN
The number of shares of our common stock to be outstanding immediately after this offering is based on 71,507,832 shares of our common stock outstanding as of April 30, 2015, and excludes as of that date:	

n 4,351,450 shares issuable upon the exercise of outstanding warrants with a weighted-average exercise price of \$9.01 per share;

- n 7,692,759 shares issuable upon the exercise of outstanding stock options with a weighted-average exercise price of \$4.52 per share;
- n 66,328 nonvested shares;
- n 333,333 shares issuable upon the conversion of our outstanding shares of Series A-1 Convertible Preferred Stock;
- n 167,000 shares available under our Employee Stock Purchase Plan;
- n 174,224 shares issuable under our Directors' Deferred Compensation Plan; and
- n 839,376 shares reserved for future issuance under our 2009 Equity Incentive Plan, as amended, or the 2009 Plan, or an additional 4,000,000 shares reserved for future issuance under our 2009 Plan for which our board of directors approved an increase in March 2015, subject to approval by our stockholders at our 2015 annual meeting of stockholders.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriters of their option to purchase additional shares.

Table of Contents

CAUTIONARY NOTE ABOUT FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and therein and other written and oral statements we make from time to time contain certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. You can identify these forward-looking statements by the fact they use words such as could, expect, anticipate, estimate, target, may, project, guidance, intend, plan, believe, will, potential, opportunity, future, and other terms of similar meaning and expression in connection with any discussion of future operating or financial performance. You can also identify forward-looking statements by the fact that they do not relate strictly to historical or current facts. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes to differ materially from current expectations. These statements are likely to relate to, among other things, our use of proceeds from this offering, our business strategy, our research and development, our product development efforts, including related regulatory filings, our ability to commercialize our product candidates, the activities of our licensees, our prospects for initiating partnerships or collaborations, the timing of the introduction of products, the effect of new accounting pronouncements, uncertainty regarding our future operating results and our profitability, anticipated sources of funds as well as our plans, objectives, expectations and intentions.

Although we believe we have been prudent in our plans and assumptions, no assurance can be given that any goal or plan set forth in forward-looking statements can be achieved and readers are cautioned not to place undue reliance on such statements, which speak only as of the date made. We undertake no obligation to release publicly any revisions to forward-looking statements as a result of new information, future events or otherwise, except as required by law.

We have included more detailed descriptions of these risks and uncertainties and other risks and uncertainties applicable to our business that we believe could cause actual results to differ materially from any forward-looking statement in the Risk Factors sections of this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein including, but not limited to, the risk factors incorporated by reference from our filings with the SEC. We encourage you to read those descriptions carefully. We caution investors not to place significant reliance on forward-looking statements; such statements need to be evaluated in light of all the information contained and incorporated by reference in this prospectus supplement and the accompanying prospectus. Furthermore, the statements speak only as of the date of each document, and we undertake no obligation to update or revise these statements, except as required by law.

Oncophage®, Stimulon®, Retrocyte Display and SECANT® are trademarks of Agenus Inc. and its subsidiaries. All rights reserved.

Table of Contents

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully review the risks and uncertainties described below, in the accompanying prospectus and in the documents incorporated by reference herein and therein including, but not limited to, the risks included in our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2015. The risks described in these documents are not the only ones we face, but those that we currently consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance and historical trends should not be used to anticipate results or trends in future periods. Please also read carefully the section above entitled Cautionary Note About Forward-Looking Statements.

Risks Related to this Offering

You will experience immediate and substantial dilution in the net tangible book value per share of the common stock you purchase.

Since the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of \$ per share, if you purchase shares in this offering, you will suffer immediate and substantial dilution of \$ per share in the net tangible book value of the common stock. See the section entitled Dilution below for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

You may experience future dilution as a result of future equity offerings and exercise of outstanding options and nonvested warrants.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering. As of March 31, 2015, 809,370 shares of common stock were reserved for future issuance under our stock option plan. As of that date, there were also options outstanding to purchase 7,834,555 shares of our common stock and warrants outstanding to purchase approximately 4,351,450 shares of our common stock. You will incur dilution upon exercise of any outstanding stock options or warrants.

We will have broad discretion in the use of the net proceeds from this offering and may allocate the net proceeds from this offering in ways that you and other stockholders may not approve.

Our management will have broad discretion in the use of the net proceeds, including for any of the purposes described in the section entitled Use of Proceeds, 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 from their currently intended use. The failure of our management to use these funds effectively could have a material adverse effect on our business, cause the market price of our common stock to decline and delay the development of our technologies. Pending their ultimate use, we intend to invest the net proceeds in short-term, investment-grade,

interest-bearing instruments. These investments may not yield a favorable return to our stockholders.

Future sales of our common stock in the public market or other financings could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market, the perception that these sales might occur or other financing transactions could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. Although there can be no assurance that all shares being offered under this prospectus will be sold or the price at which any such shares might be sold, assuming that an aggregate of shares of our common stock are sold in this offering at a price of \$6.69 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on May 19, 2015, then

S-5

Table of Contents

upon completion of this offering, based on our shares outstanding as of April 30, 2015, we will have outstanding an aggregate of _____ shares of common stock, assuming no exercise of outstanding stock options or warrants or conversion of any shares of our outstanding Series A-1 Convertible Preferred Stock. A substantial majority of the outstanding shares of our common stock are, and all of the shares sold in this offering upon issuance will be, freely tradable without restriction or further registration under the Securities Act of 1933, as amended, or the Securities Act, unless these shares are owned or purchased by affiliates as that term is defined in Rule 144 under the Securities Act. In addition, shares of common stock issuable upon exercise of outstanding options and shares reserved for future issuance under our incentive stock plan will be eligible for sale in the public market to the extent permitted by applicable vesting requirements and, in some cases, subject to compliance with the requirements of Rule 144. Similarly, shares of our common stock issuable upon exercise of warrants and conversion of our Series A-1 Convertible Preferred Stock will also generally be freely sold in the public market upon issuance, subject to restrictions under the securities laws. As a result, these shares can be freely sold in the public market upon issuance, subject to restrictions under the securities laws.

Risks Related to our Business

If we incur operating losses for longer than we expect, or we are not able to raise additional capital, we may be unable to continue our operations, or we may become insolvent.

Our net losses for the years ended December 31, 2014, 2013, and 2012, were \$42.5 million, \$30.1 million, and \$11.3 million, respectively. During three months ended March 31, 2015, we generated a net loss of \$18.7 million.

We expect to incur additional losses over the next several years as we continue research and clinical development of our technologies and pursue partnering opportunities, regulatory strategies, commercialization, and related activities. Furthermore, our ability to generate cash from operations is dependent on the success of our licensees and collaborative partners, as well as the likelihood and timing of new strategic licensing and partnering relationships and/or successful development and commercialization of CPM product candidates, including through our collaboration with Incyte, our HSP-based vaccines, and vaccines containing QS-21 Stimulon. From our inception through March 31, 2015, we have incurred net losses totaling \$710.0 million.

On March 31, 2015, we had \$79.3 million in cash and cash equivalents. We believe that, based on our current plans and activities, our working capital resources at March 31, 2015, plus anticipated proceeds from this offering, will be sufficient to satisfy our liquidity requirements into 2017. We expect to attempt to raise additional funds in advance of depleting our current funds although additional funding may not be available on favorable terms, or at all. For the three months ended March 31, 2015, our average monthly cash provided by operating activities was approximately \$1.1 million. This average monthly cash provided by operating activities primarily resulted from one-time payments received under the collaboration agreement and therefore our net cash provided by operations for the quarter ended March 31, 2015 is not indicative of future results.

We have financed our operations primarily through the sale of equity and debt securities. In order to finance future operations, we will be required to raise additional funds in the capital markets, through arrangements with collaborative partners, such as our global alliance with Incyte, or from other sources. Additional financing may not be available on favorable terms, or at all. If we are unable to raise additional funds when we need them or if we incur operating losses for longer than we expect, we may not be able to continue some or all of our operations, or we may become insolvent. We also may be forced to license or sell technologies to others under agreements that are on unfavorable terms or allocate to third parties substantial portions of the potential value of these technologies.

There are a number of factors that will influence our future capital requirements, including, without limitation, the following:

- n the number and characteristics of the product candidates we pursue;
- n our ability to successfully develop, manufacture and commercialize CPM product candidates, including pursuant to our collaboration agreement with Incyte;
- n the scope, progress, results and costs of researching and developing our future product candidates, and conducting pre-clinical and clinical trials, including with respect to our GITR and OX40 antibody programs, for which we have agreed to share all costs and profits with Incyte on a 50:50 basis;

S-6

Table of Contents

- n the timing of, and the costs involved in, obtaining regulatory approvals for our and our licensees' product candidates;
- n the cost of manufacturing;
- n our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such arrangements;
- n the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing our intellectual property rights;
- n the costs associated with any successful commercial operations; and
- n the timing, receipt and amount of sales of, or royalties on, our future products and those of our partners, if any.

General economic conditions in the United States economy and abroad may have a material adverse effect on our liquidity and financial condition, particularly if our ability to raise additional funds is impaired. The ability of potential patients and/or health care payers to pay for our products could also be adversely impacted, thereby limiting our potential revenue. In addition, any negative impacts from any deterioration in the credit markets on our collaborative partners could limit potential revenue from our product candidates.

If we default on certain of our outstanding debt instruments and the repayment of such indebtedness is accelerated, our liquidity could be materially and adversely affected.

In February 2015, we exchanged the senior subordinated promissory notes that we issued in 2013 for new senior subordinated promissory notes in the aggregate principal amount of \$5.0 million with annual interest at 8%, and we issued an additional \$9.0 million principal amount of such notes, or the 2015 Subordinated Notes. The 2015 Subordinated Notes are due February 2018 and include default provisions which allow for the acceleration of the principal payment of the 2015 Subordinated Notes in the event we become involved in certain bankruptcy proceedings, become insolvent, fail to make a payment of principal or (after a grace period) interest on the 2015 Subordinated Notes, default on other indebtedness with an aggregate principal balance of \$13.5 million or more if such default has the effect of accelerating the maturity of such indebtedness, or become subject to a legal judgment or similar order for the payment of money in an amount greater than \$13.5 million if such amount will not be covered by third-party insurance.

If we default on the 2015 Subordinated Notes and the repayment of such indebtedness is accelerated, our liquidity could be materially and adversely affected.

Our ability to satisfy our obligations under this indebtedness will depend upon our future performance, which is subject to many factors, including the factors identified in this "Risk Factors" section and other factors beyond our control. If we do not have sufficient cash on hand to service our indebtedness, we may be required, among other things, to:

- n seek additional financing in the debt or equity markets;
- n refinance or restructure all or a portion of our indebtedness;
- n sell, out-license, or otherwise dispose of assets; and/or

n reduce or delay planned expenditures on research and development and/or commercialization activities. Such measures might not be sufficient to enable us to make principal and interest payments. In addition, any such financing, refinancing, or sale of assets might not be available on favorable terms, if at all.

We are dependent upon our collaboration with Incyte to further develop, manufacture and commercialize CPM antibodies against certain targets using our proprietary antibody discovery platforms. If we or Incyte fail to perform as expected, the potential for us to generate future revenues under the collaboration would be significantly reduced, the development and/or commercialization of these CPM antibodies may be terminated or substantially delayed, and our business would be severely harmed.

Under the terms of our collaboration agreement with Incyte, we and Incyte have created a joint steering committee that oversees and manages worldwide regulatory, development, manufacturing and commercialization activities for our CPM antibody product candidates with equal representation from both parties. We anticipate that, for each program, Agenus will serve as the lead for pre-clinical development activities through the filing of an investigational new drug application, or IND, and Incyte will serve as the lead for clinical development activities. Accordingly, the

S-7

Table of Contents

timely and successful completion by Incyte of clinical development activities will significantly affect the timing and amount of any revenues we may receive under the collaboration agreement. Incyte's activities will be influenced by, among other things, the efforts and allocation of resources by Incyte, which we cannot control. If Incyte does not perform in the manner we expect or fulfill its responsibilities in a timely manner, or at all, the clinical development, manufacturing, regulatory approval and commercialization efforts related to CPM antibodies under the collaboration could be delayed or terminated, and it could become necessary for us to assume the responsibilities for the clinical development, manufacturing, regulatory approval or commercialization of the CPM antibodies at our own expense. Accordingly, there can be no assurance that any of the development, regulatory or sales milestones will be achieved, that we will receive any future milestone or royalty payments under the collaboration agreement, or that we will share in any revenues under the collaboration agreement.

In addition, our collaboration with Incyte may be unsuccessful due to other factors, including the following:

- n After February 19, 2016, Incyte may terminate the agreement or any individual program for convenience upon 12 months' notice;
- n We may have disagreements with Incyte that are not settled amicably or in our favor, particularly on the joint steering committee where Incyte will under most circumstances have the deciding vote in the event of a disagreement;
- n Incyte may change the focus of its development and commercialization efforts or prioritize other programs more highly and, accordingly, reduce the efforts and resources allocated to our collaboration;
- n Incyte may choose not to develop and commercialize CPM products, if any, in all relevant markets or for one or more indications, if at all; and
- n If Incyte is acquired during the term of our collaboration, the acquirer may have competing programs or different strategic priorities that could cause it to reduce its commitment to our collaboration.

If Incyte terminates our collaboration agreement, we would need to raise additional capital and may need to identify and come to agreement with another collaboration partner to advance our CPM programs. Even if we are able to find another partner, this effort could cause delays in our timelines and/or additional expenses, which could adversely affect our business prospects and the future of our CPM antibody product candidates.

Our CPM programs are still in pre-clinical development, and there is no guarantee that they will be successful or produce any revenues from CPM antibody product candidates, if any.

Our CPM programs are currently in pre-clinical development. Even if our pre-clinical studies produce positive results, they may not necessarily be predictive of the results of future clinical trials in humans. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical trials after achieving positive results in pre-clinical development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, pre-clinical findings made while clinical trials were underway or safety or efficacy observations made in clinical trials, including adverse events. Moreover, pre-clinical and clinical

data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in pre-clinical studies and clinical trials nonetheless failed to obtain regulatory approval. If we fail to produce positive results in future clinical trials of CPM antibodies, our business and financial prospects would be materially adversely affected.

We are undergoing significant growth, and we may encounter difficulties in managing this growth, which could disrupt our operations.

From January 1, 2014 to March 31, 2015 we increased our employee headcount from 68 to 140, 38 of whom joined us in connection with the acquisition of 4-Antibody AG (4-AB) in February 2014. In addition, through 4-AB, we also expanded our research and development activities internationally to Switzerland and Germany. In April 2015, we further expanded our antibody discovery platform through the acquisition of antibody platform assets from Celexion, LLC. We expect to continue increasing our headcount as we continue to build our research and development capabilities and integrate our acquired technology platforms. To manage this anticipated growth and expansion, we must continue to implement and improve our managerial, operational and financial systems and continue to recruit, train and retain qualified personnel. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate revenue could be reduced, and we may not be able to implement our business strategy.

S-8

Table of Contents

We may fail to realize the benefits we expect to realize as a result of the acquisition of certain assets from Celexion, LLC and/or we may suffer a loss in productivity as a result of the integration of those assets into our business.

The long-term success of the acquisition of certain assets, including the SECANT yeast display platform for the generation of novel monoclonal antibodies and efficient integration of drug targets such as CPMs, from Celexion, LLC will depend, in part, on our ability to realize the anticipated business opportunities and growth prospects from combining our proprietary Retrocyte Display platform with the SECANT platform. We may never realize these anticipated business opportunities and growth prospects. We might experience increased competition that limits our ability to expand our business, and we might not be able to capitalize on expected business opportunities, including advancing the development of CPMs. If any of these factors limit our ability to integrate the SECANT technology platform with our existing technologies successfully or on a timely basis, or to develop the business opportunities that we expect to realize from the acquisition of the SECANT technology platform, the expectations of future results of operations might not be met.

We may not receive anticipated QS-21 Stimulon revenues from our licensees or otherwise be able to monetize this asset.

We currently rely upon and expect to continue to rely upon third party licensees, particularly GlaxoSmithKline, or GSK, to develop, test, market and manufacture vaccines that utilize our QS-21 Stimulon adjuvant.

As each licensee controls its own product development process, we cannot predict our licensees' requirements for QS-21 Stimulon in the future or to what extent, if any, they will develop vaccines that use QS-21 Stimulon as an adjuvant. Our licensees may initiate or terminate programs containing QS-21 Stimulon at any time. In addition, clinical trials being conducted by our licensees may not be successful. For example, in April 2014, GSK announced the termination of a Phase 3 trial of its MAGE-A3 cancer immunotherapeutic (a vaccine containing QS-21 Stimulon) in non-small cell lung cancer, and in 2013, GSK announced the Phase 3 trial of their MAGE-A3 cancer immunotherapeutic in melanoma missed its first co-primary endpoint and that the study would continue until completion of its second co-primary endpoint, which is expected to occur in 2015. The results of these trials and other trials conducted by our licensees, as well as other factors, may cause our licensees to terminate additional programs containing QS-21 Stimulon, which could materially diminish future potential revenue from QS-21 Stimulon. In addition, even if our licensees successfully complete clinical trials with vaccine candidates using QS-21 Stimulon there is no guarantee that these products will obtain regulatory approval or, if so approved, will generate any future milestones or royalty payments.

We are currently exploring the possibility of monetizing all or part of the potential royalties we are entitled to receive from our QS-21 partners, but there is no guarantee that we will be able to do so at all, or on favorable terms.

Any inability to receive anticipated revenues, or a reduction in revenues, generated from QS-21 Stimulon, or otherwise monetize this asset could have a material adverse effect on our business, financial condition and results of operations.

Our HSP peptide-based platform for infectious diseases is in early stage development, and there is no guarantee that a product candidate will progress from this platform.

In June 2014, we reported positive results from a Phase 2 trial with our HerpV vaccine candidate for genital herpes, which includes QS-21 Stimulon. While the HerpV Phase 2 met its formal endpoints, it is unclear that the magnitude of the effect on viral load would be sufficient to significantly reduce the incidence, severity, or duration of herpetic lesions or reduce the risk of viral transmission. Although we would consider potential partnering relationships for the

further development of our HerpV program, we are not currently engaged in any discussions with any such potential partners, and we do not currently expect to advance this program into a Phase 3 trial. We are currently in the process of evaluating the broader application of our HSP peptide-based vaccines beyond genital herpes, but there is no guarantee that a product candidate will progress from this platform. Furthermore, it is possible that research and discoveries by others will render any product candidate obsolete or noncompetitive.

We may not be able to advance clinical development or commercialize Prophage Series vaccines or realize any benefits from this program without a partner or an alternative means of financing.

The probability of future clinical development efforts leading to marketing approval and commercialization of Prophage Series vaccines is highly uncertain. Prophage Series vaccines have been in clinical development for over 15 years, including multiple Phase 1 and 2 trials in eight different tumor types as well as randomized Phase 3 trials in metastatic melanoma and adjuvant renal cell carcinoma. To date, none of our clinical trials with Prophage Series vaccines has resulted in a marketing approval, except in Russia where commercialization of the approved product was unsuccessful. Although we hope to initiate a Phase 3 clinical trial in newly diagnosed GBM in 2015, due to our limited resources and our corporate priorities, we do not expect to support on-going clinical studies with Prophage

Series vaccines or perform additional studies without the help of a partner or alternative means of financing.

Table of Contents

We do not currently sponsor any on-going clinical trials with Prophage Series vaccines and therefore we lack the ability to control trial design, timelines and data availability. Current and future studies may eventually be terminated due to, among other things, slow enrollment, lack of probability that they will yield useful translational and/or efficacy data, lengthy timelines, or the unlikelihood that results will support timely or successful regulatory filings. Currently, the only actively enrolling Prophage Series vaccine clinical study is a Phase 2 trial of Prophage Series vaccine in combination with bevacizumab in patients with surgically resectable recurrent glioma. This trial is being conducted under the sponsorship of the Alliance for Clinical Trials in Oncology, a cooperative group of the National Cancer Institute. To date, clinical site activation and patient enrollment have not met expectations, which could curtail the viability of sustaining the trial. Furthermore, potential changes in clinical practices trending away from the administration of bevacizumab for the treatment of recurrent glioma could exacerbate enrollment issues and/or render the trial design impractical. In January 2014, we initiated a randomized Phase 2 trial with Prophage Series vaccine and Bristol-Myers Squibb's ipilimumab, for the treatment of Stage III and IV metastatic melanoma. This study is being sponsored by an investigator at the University of Texas and, although the investigator-held IND was activated to allow initiation of the trial, patient enrollment has not yet begun. The design of this study protocol was recently modified to incorporate a non-randomized trial of Prophage Series vaccine in combination with ipilimumab with a reference to prospective comparative patients treated with ipilimumab only. This redesign may enable us to more quickly evaluate safety and immunologic correlates of responders in patients with metastatic melanoma. While we believe the combination of Prophage Series vaccines and ipilimumab has the potential to trigger a more effective immune response against the tumor than ipilimumab alone, there is no guarantee that this trial will be completed or that it will yield useful translational and/or efficacy data.

Changes in our manufacturing strategies, manufacturing problems, or increased demand may cause delays, unanticipated costs, or loss of revenue streams within or across our programs.

Our CPM antibody programs, including those partnered with Incyte, will require substantial manufacturing development and investment to progress. The CPM antibody programs are pre-clinical, and we have only recently initiated the development of the reagents, cell lines and systems required to manufacture our antibody candidates. If these development-stage efforts are delayed or do not produce the desired outcomes, this will cause delays in development timelines and increased costs, which may cause us to limit the size and scope of our efforts and studies. In addition, our staff has limited experience in the manufacture and development of the CPM antibody programs and we have recruited or are recruiting additional staff with expertise in these areas. We also currently utilize consultants and advisors to assist advancing these operations. We rely on contract manufacturing organizations, or CMOs, and contract research organizations, or CROs, to support our CPM antibody programs. In the future, we may need to secure additional manufacturing capacity with our current or additional CMOs. Such an effort could divert resources away from the CPM antibody programs and lead to delays in the development of product candidates. We may also need to develop or secure later phase and/or commercial manufacturing capabilities, all of which would cause us to incur additional costs and risk. In the event that our CPM antibody programs require progressively larger production capabilities, our options for qualified CMOs may become more limited. In addition, while we currently have our own cGMP manufacturing facility in Lexington, MA, our facility is not currently configured or equipped to adequately support manufacturing of the required cell lines or the downstream production of cGMP antibody product candidates.

We currently manufacture our Prophage Series vaccines in our Lexington, MA facility. Manufacturing of the Prophage Series vaccines is complex, and various factors could cause delays or an inability to supply the vaccine. Deviations in the processes controlling manufacture could result in production failures. Furthermore, we have limited financial, personnel, and manufacturing resources and there is no assurance that we will be able to allocate resources necessary for the continued manufacturing of Prophage Series vaccines in light of competing corporate priorities. In addition, regulatory bodies may require us to make our manufacturing facility a single product facility. In such an instance, we would no longer have the ability to manufacture Prophage Series vaccines in addition to other product

candidates in our current facility.

We have given our corporate QS-21 Stimulon licensees, GSK and Janssen Sciences Ireland UC, manufacturing rights for QS-21 Stimulon for use in their product programs. If they or their third party contract manufacturers encounter problems with QS-21 Stimulon manufacturing, any of their programs containing QS-21 Stimulon could be delayed or terminated, and this could have an adverse effect on our license fees, milestone payments and royalties that we may otherwise receive from these programs. We have retained the right to manufacture QS-21 for ourselves and third parties, although no other such programs are anticipated to bring us substantial revenues in the near future, if ever.

S-10

Table of Contents

Our ability to efficiently manufacture our products is contingent upon a CMO's ability to ramp up production in a timely manner without the benefit of years of experience and familiarity with the processes, which we may not be able to adequately transfer.

We currently rely upon and expect to continue to rely upon third parties, potentially including our collaborators or licensees, to produce materials required to support our product candidates, pre-clinical studies, clinical trials, and commercial efforts. A number of factors could cause production interruptions at either our manufacturing facility or the facilities of our CMOs or suppliers, including equipment malfunctions, labor or employment retention problems, natural disasters, power outages, terrorist activities, or disruptions in the operations of our suppliers. Alternatively, there is the possibility we may have excess manufacturing capacity if product candidates do not progress as planned.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured products ourselves, including reliance on the third party for regulatory compliance, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control, and the possibility of termination or non-renewal of the agreement by the third party, based on its own business priorities, at a time that is costly or inconvenient for us.

Biopharmaceutical manufacturing is also subject to extensive government regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Our facilities and quality systems and the facilities and quality systems of some or all of our third party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of product candidates. In addition, facilities are subject to on-going inspections, and minor changes in manufacturing processes may require additional regulatory approvals, either of which could cause us to incur significant additional costs and lose revenue.

Risks associated with doing business internationally could negatively affect our business.

We have research and development operations in Switzerland and Germany. We have in the past, and may continue to pursue pathways to develop and commercialize our product candidates in non-U.S. jurisdictions. Various risks associated with foreign operations may impact our success. Possible risks of foreign operations include fluctuations in the value of foreign and domestic currencies, disruptions in the import, export, and transportation of patient tumors and our products or product candidates, the product and service needs of foreign customers, difficulties in building and managing foreign relationships, the performance of our licensees or collaborators, geopolitical instability, unexpected regulatory, economic, or political changes in foreign markets and limitations on the flexibility of our operations and costs imposed by local labor laws. For example, our Oncophage® vaccine is approved for sale in Russia, but we have not and do not expect to receive any revenues from sales in Russia. See Risk Factors- Even if we receive marketing approval for our product candidates, such product approvals could be subject to restrictions or withdrawals. Regulatory requirements are subject to change.

Our competitors in the biotechnology and pharmaceutical industries may have superior products, manufacturing capability, selling and marketing expertise and/or financial and other resources.

Our product candidates and the product candidates in development by our collaborative partners may fail because of competition from major pharmaceutical companies and specialized biotechnology companies that market products, or that are engaged in the development of product candidates, directed at cancer, infectious diseases and degenerative disorders. Many of our competitors, including large pharmaceutical companies, have greater financial and human

resources and more experience than we do. Our competitors may:

- n commercialize their product candidates sooner than we commercialize our own;
- n develop safer or more effective therapeutic drugs or preventive vaccines and other therapeutic products;
- n implement more effective approaches to sales and marketing and capture some of our potential market share;
- n establish superior intellectual property positions;
- n discover technologies that may result in medical insights or breakthroughs, which render our drugs or vaccines obsolete, possibly before they generate any revenue, if ever; or
- n adversely affect our ability to recruit patients for our clinical trials.

S-11

Table of Contents

There is no guarantee that our products or product candidates will be able to compete with potential future products being developed by our competitors.

We have CPM antibody programs currently in pre-clinical development targeting GITR, OX40, CTLA-4, LAG-3, TIM-3 and PD-1. We are aware of many companies that have antibody-based products on the market or in clinical development that are directed to the same biological target as some of our programs, including, without limitation, the following: (1) Bristol-Myers Squibb markets ipilimumab, an anti-CTLA-4 antibody, and nivolumab, an anti-PD1 antibody, (2) Merck has an approved anti-PD1 antibody in the United States, (3) Ono Pharmaceuticals has an approved anti-PD1 antibody in Japan, (4) Medimmune has anti-CTLA-4, OX-40 and PD1 antibodies in development, (5) Curetech has an anti-PD1 antibody in development, and (6) Pfizer has an anti-CTLA-4 antibody in development. Tesaro also has antibody programs targeting PD-1, TIM-3 and LAG-3, which include both monospecific and dual reactive antibody drug candidates. There is no guarantee that our antibody product candidates will be able to compete with those under development by our competitors.

We are aware of compounds that claim to be comparable to QS-21 Stimulon that are being used in clinical trials. Several other vaccine adjuvants are in development and could compete with QS-21 Stimulon for inclusion in vaccines in development. These adjuvants include, but are not limited to, oligonucleotides, under development by Pfizer, Idera, Colby, and Dynavax, MF59, under development by Novartis, IC31, under development by Intercell, and MPL, under development by GSK. In the past, we have provided QS-21 Stimulon to other entities under materials transfer arrangements. In at least one instance, it is possible that this material was used unlawfully to develop synthetic formulations and/or derivatives of QS-21. In addition, companies such as Adjuvance Technologies, Inc., CSL Limited, and Novavax, Inc., as well as academic institutions and manufacturers of saponin extracts, are developing saponin adjuvants, including derivatives and synthetic formulations. These sources may be competitive for our ability to execute future partnering and licensing arrangements involving QS-21 Stimulon. The existence of products developed by these and other competitors, or other products of which we are not aware or which other companies may develop in the future, may adversely affect the marketability of products we develop.

We are also aware of a third party that manufactures pre-clinical material purporting to be comparable to QS-21 Stimulon. The claims being made by this third party may create marketplace confusion and have an adverse effect on the goodwill generated by us and our partners with respect to QS-21 Stimulon. Any diminution of this goodwill may have an adverse effect on our ability to commercialize this technology, either alone or with a third party.

In competition with our Prophage Series product candidates, Genentech markets bevacizumab, and Eisai and Arbor Pharmaceuticals market carmustine. In addition, TVAX Biomedical and Stemline Therapeutics are developing immunotherapy candidates TVI-Brain-1 and SL-701, respectively, for recurrent glioma. Schering Corporation, a subsidiary of Merck, markets temozolamide for treatment of patients with newly diagnosed glioma. Other companies are developing vaccine candidates for the treatment of patients with newly diagnosed glioma, such as ImmunoCellular Therapeutics (ICT-107), Northwest Biotherapeutics (DC-Vax), Immatics (IMA-950), Activartis Biotech (GBM-Vax), Annias Immunotherapeutics (CMV Vaccine) and Celldex (CDX-110). Other companies may begin development programs as well.

If vaccines from our Prophage Series vaccines are developed in other indications, they could face additional competition in those indications. In addition, and prior to regulatory approval, our Prophage Series vaccines and all of our other product candidates may compete for access to patients with other products in clinical development, with products approved for use in the indications we are studying, or with off-label use of products in the indications we are studying. We anticipate that we will face increased competition in the future as new companies enter markets we seek to address and scientific developments surrounding immunotherapy and other traditional cancer therapies continue to accelerate.

Our future growth depends on our ability to successfully identify, develop, acquire or in-license technologies, products and product candidates; otherwise, we may have limited growth opportunities.

An important part of our business strategy is to continue to develop a pipeline of product candidates by developing, acquiring or in-licensing products, businesses or technologies that we believe are a strategic fit with our existing business. However, these business activities may entail numerous operational and financial risks, including:

- n difficulty or inability to secure financing to fund development activities for such development, acquisition or in-licensed products or technologies;

S-12

Table of Contents

- n incurrence of substantial debt or dilutive issuances of securities to pay for development, acquisition or in-licensing of new technologies, products or product candidates;
- n disruption of our business and diversion of our management's time and attention;
- n higher than expected development, acquisition or in-license and integration costs;
- n exposure to unknown liabilities;
- n difficulty and cost in combining the technologies, operations and personnel of any acquired businesses with our technologies, operations and personnel, including without limitation, the assets we recently acquired from Celexion, LLC;
- n inability to retain key employees of any acquired businesses;
- n difficulty in managing multiple product development programs; and
- n inability to successfully develop new products or clinical failure.

We have limited resources to identify and execute the development, acquisition or in-licensing of products, businesses and technologies and integrate them into our current infrastructure. We may compete with larger pharmaceutical companies and other competitors in our efforts to establish new collaborations, and/or acquire, in-license, and/or advance new product candidates. These competitors likely will have access to greater financial resources than us and may have greater expertise in identifying and evaluating new opportunities. Moreover, we may devote resources to potential development, acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts.

Failure to enter into and/or maintain significant licensing, distribution and/or collaboration agreements on favorable terms to us may hinder or cause us to cease our efforts to develop and commercialize our product candidates, increase our development timelines, and/or increase our need to rely on partnering or financing mechanisms, such as sales of debt or equity securities, to fund our operations and continue our current and anticipated programs.

As previously noted, our ability to advance our CPM programs depends in part on collaborative agreements such as our collaboration with Incyte. See Risk Factors Risks Related to Our Business We are dependent upon our collaboration with Incyte to further develop, manufacture and commercialize CPM antibodies against certain targets using our proprietary antibody discovery platforms. If we or Incyte fail to perform as expected, the potential for us to generate future revenues under the collaboration would be significantly reduced, the development and/or commercialization of these CPM antibodies may be terminated or substantially delayed, and our business would be severely harmed. In addition, we have been engaged in efforts to enter into licensing, distribution and/or collaborative agreements with one or more pharmaceutical or biotechnology companies to assist us with development and/or commercialization of our other product candidates. If we are successful in entering into such agreements, we may not

be able to negotiate agreements with economic terms similar to those negotiated by other companies. We may not, for example, obtain significant upfront payments, substantial royalty rates or milestones. If we fail to enter into any such agreements, our efforts to develop and/or commercialize our products or product candidates may be undermined. In addition, if we do not raise funds through any such agreements, we will need to rely on other financing mechanisms, such as sales of debt or equity securities, to fund our operations. Such financing mechanisms, if available, may not be sufficient or timely enough to advance our programs forward in a meaningful way in the short-term.

While we have been pursuing these business development efforts for several years for our Prophage Series vaccine, we have not entered into a substantial agreement other than the agreement with NewVac which was unsuccessful and expired in 2014. In addition, other companies may not be interested in pursuing patient-specific vaccines like our Prophage Series vaccines, and many other companies have been and may continue to be unwilling to commit to an agreement prior to receipt of additional clinical data, if at all.

Because we rely on collaborators and licensees for the development and commercialization of most of our product candidate programs, these programs may not prove successful, and/or we may not receive significant payments from such parties.

Part of our strategy is to develop and commercialize a majority of our product candidates by continuing or entering into arrangements with academic, government, or corporate collaborators and licensees. Our success depends on our ability to negotiate such agreements on favorable terms and on the success of the other parties in performing research, pre-clinical and clinical testing, completing regulatory applications, and commercializing product candidates. Our research, development, and commercialization efforts with respect to antibody candidates from the

Table of Contents

Retrocyte Display and SECANT technology platforms are, in part, contingent upon the participation of institutional and corporate collaborators. For example, 4-AB has or has had collaborative arrangements with Ludwig Cancer Research, or LCR, and Brazil-based Recepta Biopharma SA, or Recepta, among others. In December 2014, we entered into a new license agreement with LCR, which replaced the prior agreement for some of our target programs. We are in continued discussions with LCR and Recepta with respect to certain of our other target programs. If we are not able to come to agreement on terms or maintain and optimize these arrangements, as well as advance other current or potential collaborations on terms favorable to us, this could have a negative impact on our operations. In February 2015 we began a broad collaboration with Incyte to pursue the discovery and development of CPMs. See Risk Factors-Risks Related to our Business-We are dependent upon our collaboration with Incyte to further develop, manufacture and commercialize CPM antibodies against certain targets using our proprietary antibody discovery platforms. If we or Incyte fail to perform as expected, the potential for us to generate future revenues under the collaboration would be significantly reduced, the development and/or commercialization of these CPM antibodies may be terminated or substantially delayed, and our business would be severely harmed.

In addition, substantially all product candidates containing QS-21 Stimulon depend on the success of our collaborative partners or licensees, and our relationships with these third parties. Such product candidates depend on our collaborators and licensees successfully enrolling patients and completing clinical trials, being committed to dedicating the resources necessary to advance these product candidates, obtaining regulatory approvals, and successfully manufacturing and commercializing product candidates.

To date, the development of Prophage Series vaccine for the treatment of patients with glioma has been driven by investigator sponsored initiatives, spear-headed in large part by Dr. Andrew Parsa in conjunction with the Alliance for Clinical Trials in Oncology, a National Cancer Institute cooperative group, or NCI, which is sponsoring a Phase 2 clinical trial of this product candidate in this indication. On April 13, 2015, Dr. Andrew Parsa passed away unexpectedly. While several other investigators and the NCI Alliance have supported and expressed they will continue to support the Prophage Series glioma programs, it is possible that these investigator sponsored initiatives could be delayed or even terminated as a result of Dr. Parsa's passing. Furthermore, when our licensees or third party collaborators sponsor clinical trials using our product candidates, we cannot control the timing of enrollment, data readout, or quality of such trials or related activities. In addition, substantially all product candidates containing QS-21 Stimulon depend on the success of our collaborative partners or licensees, and our relationships with these third parties. Such product candidates depend on our collaborators and licensees successfully enrolling patients and completing clinical trials, being committed to dedicating the resources to advance these product candidates, obtaining regulatory approvals, and successfully manufacturing and commercializing product candidates. We previously granted NewVac an exclusive license to manufacture, market and sell Oncophage® in the Russian Federation and certain other CIS countries, but the relationship was unsuccessful and expired in 2014 with no benefit to us.

Development activities for our collaborative programs may fail to produce marketable products due to unsuccessful results or abandonment of these programs, failure to enter into future collaborations or license agreements, or the inability to manufacture product supply requirements for our collaborators and licensees. Several of our agreements also require us to transfer important rights and regulatory compliance responsibilities to our collaborators and licensees. As a result of these collaborative agreements, we will not control the nature, timing, or cost of bringing these product candidates to market. Our collaborators and licensees could choose not to, or be unable to, devote resources to these arrangements or adhere to required timelines, or, under certain circumstances, may terminate these arrangements early. They may cease pursuing product candidates or elect to collaborate with different companies. In addition, these collaborators and licensees, outside of their arrangements with us, may develop technologies or products that are competitive with those that we are developing. From time to time, we may also become involved in disputes with our collaborators or licensees. Such disputes could result in the incurrence of significant expense, or the termination of collaborations. We may be unable to fulfill all of our obligations to our collaborators, which may result

in the termination of collaborations. As a result of these factors, our strategic collaborations may not yield revenue. Furthermore, we may be unable to enter into new collaborations or enter into new collaborations on favorable terms. Failure to generate significant revenue from collaborations could increase our need to fund our operations through sales of debt or equity securities and would negatively affect our business prospects.

S-14

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

We have generated significant net operating loss carryforwards, or NOLs, as a result of our incurrence of losses since inception. We generally are able to carry NOLs forward to reduce taxable income in future years. However, our ability to utilize the NOLs is subject to the rules of Section 382 of the Internal Revenue Code of 1986, as amended.

Section 382 generally restricts the use of NOLs after an ownership change. An ownership change occurs if, among other things, the stockholders (or specified groups of stockholders) who own or have owned, directly or indirectly, 5% or more of a corporation's common stock or are otherwise treated as 5% stockholders under Section 382 and the United States Treasury Department regulations promulgated thereunder increase their aggregate percentage ownership of that corporation's stock by more than 50 percentage points over the lowest percentage of the stock owned by these stockholders over the applicable testing period. In the event of an ownership change, Section 382 imposes an annual limitation on the amount of taxable income a corporation may offset with NOL carry forwards. This annual limitation is generally equal to the product of the value of the corporation's stock on the date of the ownership change, multiplied by the long-term tax-exempt rate published monthly by the Internal Revenue Service. Any unused annual limitation may be carried over to later years until the applicable expiration date for the respective NOL carry forwards. We may have experienced an ownership change within the meaning of Section 382 in the past and there can be no assurance that we have not experienced additional ownership changes. As a result, our NOLs may be subject to limitations and we may be required to pay taxes earlier and in larger amounts than would be the case if our NOLs were freely usable. Any such limitation could have a material adverse effect on our results of operations in future years. We have not completed a study to assess whether an ownership change for purposes of Section 382 has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such a study.

Our internal computer systems, or those of our third-party clinical research organizations, licensees, collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption in our business and operations.

Despite the implementation of security measures, our internal computer systems and those of our current and future clinical research organizations, licensees, collaborators and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we are not aware of any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significant costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our drug candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development and commercialization of our product candidates could be delayed.

We are highly reliant on our Chief Executive Officer, Chief Scientific Officer and other members of our management team. In addition, we have limited internal resources and if we fail to recruit and/or retain the services of key employees and external consultants as needed, we may not be able to achieve our strategic and operational objectives.

Both Garo H. Armen, Ph.D., the Chairman of our Board of Directors and our Chief Executive Officer who co-founded the Company in 1994, and Dr. Robert Stein, our Chief Scientific Officer who joined the Company in February 2014, are integral to building our company and developing our technology. If either Dr. Armen or Dr. Stein is unable or

unwilling to continue his relationship with Agenus, our business may be adversely impacted.

Effective December 31, 2005, we entered into an employment agreement with Dr. Armen. Subject to the earlier termination as provided in the agreement, the agreement had an original term of one year and is automatically extended thereafter for successive terms of one year each, unless either party provides notice to the other at least ninety days prior to the expiration of the original or any extension term. We do not currently have an employment agreement with Dr. Stein. Dr. Armen and Dr. Stein play important roles in our day-to-day activities. We do not carry key employee insurance policies for Dr. Armen, Dr. Stein or any other employee.

Our future growth success depends to a significant extent on the skills, experience and efforts of our executive officers and key members of our clinical and scientific staff. We face intense competition for qualified individuals

S-15

Table of Contents

from other pharmaceutical, biopharmaceutical and biotechnology companies, as well as academic and other research institutions. We may be unable to retain our current personnel or attract or assimilate other highly qualified management and clinical personnel in the future on acceptable terms. The loss of any or all of these individuals could harm our business and could impair our ability to support our collaboration with Incyte or to support our expected growth. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate revenue could be reduced and we may not be able to implement our business strategy.

We rely on a small staff of highly trained and experienced senior management and scientific, administrative and operations personnel and consultants to conduct our business in certain key areas of our organization.

Reduction in expenses and resulting changes to our compensation and benefit programs have reduced the competitiveness of these programs and thereby increased employee retention risk. The competition for qualified personnel in the biotechnology field is intense, and if we are not able to continue to attract and retain qualified personnel and/or maintain positive relationships with our outside consultants, we may not be able to achieve our strategic and operational objectives.

Risks Related to Regulation of the Biopharmaceutical Industry

The drug development and approval process is uncertain, time-consuming, and expensive.

Clinical development, including pre-clinical testing and the process of obtaining and maintaining regulatory approvals for new therapeutic products, is lengthy, expensive, and uncertain. As of March 31, 2015, we have spent approximately 20 years and \$310.9 million on our research and development program in heat shock proteins for cancer. The development and regulatory approval process also can vary substantially based on the type, complexity, and novelty of the product. We must provide regulatory authorities with manufacturing, product characterization, and pre-clinical and clinical data demonstrating that our product candidates are safe and effective before they can be approved for commercial sale. It may take us many years to complete our testing, and failure can occur at any stage of testing. Interim results of pre-clinical studies or clinical trials do not necessarily predict their final results, and acceptable results in early studies might not be seen in later studies. Any pre-clinical or clinical test may fail to produce results satisfactory to regulatory authorities for many reasons, including but not limited to insufficient product characterization, poor study structure conduct or statistical analysis planning, failure to enroll a sufficient number of patients or failure to prospectively identify the most appropriate patient eligibility criteria, and collectability of data. Pre-clinical and clinical data can be interpreted in different ways, which could delay, limit, or prevent regulatory approval. Negative or inconclusive results from a pre-clinical study or clinical trial, adverse medical events during a clinical trial, or safety issues resulting from products of the same class of drug could require a pre-clinical study or clinical trial to be repeated or cause a program to be terminated, even if other studies or trials relating to the program are successful. We or the FDA, other regulatory agencies, or an institutional review board may suspend or terminate human clinical trials at any time on various grounds.

The timing and success of a clinical trial is dependent on obtaining and maintaining sufficient cash resources, successful production of clinical trial material, enrolling sufficient patients in a timely manner, avoiding serious or significant adverse patient reactions, and demonstrating efficacy of the product candidate in order to support a favorable risk versus benefit profile, among other considerations. The timing and success of our clinical trials, in particular, are also dependent on clinical sites and regulatory authorities accepting each trial's protocol, statistical analysis plan, product characterization tests, and clinical data. In addition, regulatory authorities may request additional information or data that is not readily available. Delays in our ability to respond to such requests would delay, and failure to adequately address concerns would prevent, our commercialization efforts. We have encountered in the past, and may encounter in the future, delays in initiating trial sites and enrolling patients into our clinical trials.

Future enrollment delays will postpone the dates by which we expect to complete the impacted trials and the potential receipt of regulatory approval. There is no guarantee we will successfully initiate and/or complete our clinical trials.

Delays or difficulties in obtaining regulatory approvals or clearances for our product candidates may:

- n adversely affect the marketing of any products we or our licensees or collaborators develop;
- n impose significant additional costs on us or our licensees or collaborators;

S-16

Table of Contents

n diminish any competitive advantages that we or our licensees or collaborators may attain;

n limit our ability to receive royalties and generate revenue and profits; and

n adversely affect our business prospects and ability to obtain financing.

Delays or failures in our receiving regulatory approval for our product candidates in a timely manner may result in us having to incur additional development expense and subject us to having to secure additional financing. As a result, we may not be able to commercialize them in the time frame anticipated, and our business will suffer.

Even if we receive marketing approval for our product candidates, such product approvals could be subject to restrictions or withdrawals. Regulatory requirements are subject to change. Further, even if we receive marketing approval, we may not receive sufficient coverage and adequate reimbursement for our products.

Regulatory authorities generally approve products for particular indications. If an approval is for a limited indication, this limitation reduces the size of the potential market for that product. Product approvals, once granted, are subject to continual review and periodic inspections by regulatory authorities. Our operations and practices are subject to regulation and scrutiny by the United States government, as well as governments of any other countries in which we do business or conduct activities. Later discovery of previously unknown problems or safety issues, and/or failure to comply with domestic or foreign laws, knowingly or unknowingly, can result in various adverse consequences, including, among other things, possible delay in approval or refusal to approve a product, warning letters, fines, injunctions, civil penalties, recalls or seizures of products, total or partial suspension of production, refusal of the government to renew marketing applications, complete withdrawal of a marketing application, corrective action requirements, and/or criminal prosecution, withdrawal of an approved product from the market, and/or exclusion from government health care programs. Such regulatory enforcement could have a direct and negative impact on the product for which approval is granted, but also could have a negative impact on the approval of any pending applications for marketing approval of new drugs or supplements to approved applications.

Because we are a company operating in a highly regulated industry, regulatory authorities could take enforcement action against us in connection with our licensees or collaborators, and/or our business and marketing activities for various reasons. For example, the Foreign Corrupt Practices Act prohibits U.S. companies and their representatives from offering, promising, authorizing, or making payments to foreign governmental officials for the purpose of obtaining or retaining business abroad.

From time to time, new legislation is passed into law that could significantly change the statutory provisions governing the approval, manufacturing, and marketing of products regulated by the FDA and other foreign health authorities. Additionally, regulations and guidance are often revised or reinterpreted by health agencies in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted, or whether regulations, guidance, or interpretations will change, and what the impact of such changes, if any, may be. For example, the Patient Protection and Affordable Care Act and the Health Care and Education Affordability Reconciliation Act of 2010, collectively, the ACA, enacted in March 2010, substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the pharmaceutical industry. With regard to pharmaceutical products, among other things, ACA is expected to expand, increase, and change the methodology regarding industry rebates for drugs covered under Medicaid programs; impose an annual, nondeductible fee on any entity that manufactures or imports specific branded prescription drugs and biologic agents, apportioned among those entities according to market share in certain government healthcare programs; expand eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain

individuals with income at or below 133% of the federal poverty level; expand the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; create a new Patient Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and make changes to the coverage requirements under the Medicare D program.

We expect both government and private health plans to continue to require healthcare providers, including healthcare providers that may one day purchase our products, to contain costs and demonstrate the value of the therapies they provide. Even if our product candidates are approved, the commercial success of our products will depend substantially on the extent to which they are covered by third-party payors, including government health authorities and private health insurers. In the United States, no uniform policy of coverage and reimbursement for

S-17

Table of Contents

products exists among third-party payors, and coverage and reimbursement for products can differ significantly from payor to payor. If coverage and reimbursement are not available, or reimbursement is available only to limited levels, we or our collaborators may not be able to successfully commercialize our product candidates.

New data from our research and development activities, and/or resource considerations could modify our strategy and result in the need to adjust our projections of timelines and costs of programs.

Because we are focused on novel technologies, our research and development activities, including our nonclinical studies and clinical trials, involve the ongoing discovery of new facts and the generation of new data, based on which we determine next steps for a relevant program. These developments can occur with varying frequency and constitute the basis on which our business is conducted. We make determinations on an ongoing basis as to which of these facts or data will influence timelines and costs of programs. We may not always be able to make such judgments accurately, which may increase the costs we incur attempting to commercialize our product candidates. We monitor the likelihood of success of our initiatives and we may need to discontinue funding of such activities if they do not prove to be commercially feasible, due to our limited resources.

We may need to successfully address a number of technological challenges in order to complete development of our product candidates. Moreover, these product candidates may not be effective in treating any disease or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining regulatory approvals or prevent or limit commercial use.

Risks Related to Intellectual Property Rights

If we are unable to obtain and enforce patent protection for our product candidates and related technology, our business could be materially harmed.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates and technology. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to duplicate or surpass our technological achievements, eroding our competitive position in the market. Our patent applications may not result in issued patents, and, even if issued, the patents may be challenged and invalidated. Moreover, our patents and patent applications may not be sufficiently broad to prevent others from practicing our technologies or developing competing products. We also face the risk that others may independently develop similar or alternative technologies or may design around our proprietary property.

Issued patents may be challenged, narrowed, invalidated or circumvented. In addition, court decisions may introduce uncertainty in the enforceability or scope of patents owned by biotechnology companies. The legal systems of certain countries do not favor the aggressive enforcement of patents, and the laws of foreign countries may not allow us to protect our inventions with patents to the same extent as the laws of the United States. Because patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in scientific literature lag behind actual discoveries, we cannot be certain that we were the first to make the inventions claimed in our issued patents or pending patent applications, or that we were the first to file for protection of the inventions set forth in our patents or patent applications. As a result, we may not be able to obtain or maintain protection for certain inventions. Therefore, the enforceability and scope of our patents in the United States and in foreign countries cannot be predicted with certainty and, as a result, any patents that we own or license may not provide sufficient protection against competitors. We may not be able to obtain or maintain patent protection from our pending patent applications, from those we may file in the future, or from those we may license from third parties. Moreover, even if we are able to obtain patent protection, such patent protection

may be of insufficient scope to achieve our business objectives.

Patent term may be inadequate to protect our competitive position on our product candidates for an adequate amount of time. Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its effective filing date. Various extensions may be available; however the life of a patent, and the protection it affords, is limited. Without patent protection for our product candidates, we may be open to competition from generic versions of our product candidates. Furthermore, the product development timeline for biotechnology products is lengthy and it is possible that our issued patents covering our product candidates in the

S-18

Table of Contents

United States and other jurisdictions may expire prior to commercial launch. For example, if we encounter delays in our development efforts, including our clinical trials, the period of time during which we could market our product candidates under patent protection could be reduced.

Our strategy depends on our ability to identify and seek patent protection for our discoveries. This process is expensive and time consuming, and we and our current or future licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we or our current licensors, or any future licensors or licensees, may not identify patentable aspects of inventions made in the course of development and commercialization activities in time to obtain patent protection on them. Therefore, these and any of our patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, etc. If we or our current licensors, or any future licensors or licensees, fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our current licensors, or any future licensors or licensees, are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Despite our efforts to protect our proprietary rights, unauthorized parties may be able to obtain and use information that we regard as proprietary. The issuance of a patent does not ensure that it is valid or enforceable, so even if we obtain patents, they may not be valid or enforceable against third parties. In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our own patented product and practicing our own patented technology. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The patent landscape in the field of therapeutic antibody development, manufacture and commercialization is crowded. For example, we are aware of third party patents directed to methods for identifying and producing therapeutic antibodies. We are also aware of third party patents directed to antibodies to numerous targets for which we also seek to identify, develop, and commercialize antibodies, including without limitation CTLA-4, PD-1, GITR, OX40, TIM-3, and LAG-3. For example, some patents claim antibodies based on competitive binding with existing antibodies, some claim antibodies based on specifying sequence or other structural information, and some claim various methods of discovery, production, or use of such antibodies.

These or other third party patents could impact our freedom to operate in relation to our technology platforms, including Retrocyte Display and SECANT, as well as in relation to development and commercialization of antibodies identified by us as therapeutic candidates. As we discover and develop our candidate antibodies, we will continue to conduct analyses of these third party patents to determine whether we believe we might infringe them, and if so, whether they would be likely to be deemed valid and enforceable if challenged. If we determine that a license for a given patent or family of patents is necessary or desirable, there can be no guarantee that a license would be available on favorable terms, or at all. Inability to obtain a license on favorable terms, should such a license be determined to be necessary or desirable, could, without limitation, result in increased costs to design around the third party patents, delay product launch, or result in cancellation of the affected program or cessation of use of the affected technology.

Third parties may also seek to market biosimilar versions of any approved products. Alternatively, third parties may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or agency with jurisdiction may find our patents invalid and/or unenforceable. Even if we have valid and enforceable patents, these patents still may not provide protection

against competing products or processes sufficient to achieve our business objectives.

We have ownership of or exclusive rights to approximately 60 issued United States patents and approximately 120 issued foreign patents. We also have ownership of or exclusive rights to approximately 19 pending United States patent applications and approximately 40 pending foreign patent applications. However, our patents may not protect

S-19

Table of Contents

us against our competitors. Our patent positions, and those of other pharmaceutical and biotechnology companies, are generally uncertain and involve complex legal, scientific, and factual questions. The standards which the United States Patent and Trademark Office, or USPTO, uses to grant patents, and the standards which courts use to interpret patents, are not always applied predictably or uniformly and can change, particularly as new technologies develop.

Consequently, the level of protection, if any, that will be provided by our patents if we attempt to enforce them, and they are challenged, is uncertain. In addition, the type and extent of patent claims that will be issued to us in the future is uncertain. Any patents that are issued may not contain claims that permit us to stop competitors from using similar technology.

Through our acquisitions of 4-AB and certain assets of Celexion, LLC, we also own a number of patents and patent applications directed to various methods and compositions, including methods for identifying therapeutic antibodies and product candidates arising out of such entities' technology platforms. In particular, we own patents and patent applications relating to Retrocyte Display technology platform, a high throughput antibody expression platform for the identification of fully-human and humanized monoclonal antibodies. This patent family is projected to expire between 2029 and 2031. We also own patents and patent applications relating to the SECANT platform, a platform used for the generation of novel monoclonal antibodies and efficient integration of drug targets such as CPMs. This patent family is projected to expire between 2028 and 2029. In addition, as we advance our research and development efforts with our institutional and corporate collaborators, we intend to seek patent protection for newly-identified therapeutic antibodies and product candidates. We can provide no assurance that any of our patents, including the patents that were acquired along with 4-AB, will have commercial value, or that any of our existing or future patent applications, including the patent applications that were acquired with 4-AB, will result in the issuance of valid and enforceable patents.

The issued patents that cover the Prophage Series vaccines expire at various dates between 2015 and 2024. Our QS-21 Stimulon composition of matter patent family expired in 2008. Additional protection for QS-21 Stimulon in combination with other agents is provided by our other issued patents which expire between 2017 and 2022. We continue to explore means of extending the life cycle of our patent portfolio.

The patent position of pharmaceutical or biotechnology companies, including ours, is generally uncertain and involves complex legal and factual considerations. The standards which the USPTO and its foreign counterparts use to grant patents are not always applied predictably or uniformly and can change. There is also no uniform, worldwide policy regarding the subject matter and scope of claims granted or allowable in pharmaceutical or biotechnology patents. The laws of some foreign countries do not protect proprietary information to the same extent as the laws of the United States, and many companies have encountered significant problems and costs in protecting their proprietary information in these foreign countries. Outside the United States, patent protection must be sought in individual jurisdictions, further adding to the cost and uncertainty of obtaining adequate patent protection outside of the United States. Accordingly, we cannot predict whether additional patents protecting our technology will issue in the United States or in foreign jurisdictions, or whether any patents that do issue will have claims of adequate scope to provide competitive advantage. Moreover, we cannot predict whether third parties will be able to successfully obtain claims or the breadth of such claims. The allowance of broader claims may increase the incidence and cost of patent interference proceedings, opposition proceedings, post-grant review, inter partes review, and/or reexamination proceedings, the risk of infringement litigation, and the vulnerability of the claims to challenge. On the other hand, the allowance of narrower claims does not eliminate the potential for adversarial proceedings, and may fail to provide a competitive advantage. Our issued patents may not contain claims sufficiently broad to protect us against third parties with similar technologies or products, or provide us with any competitive advantage.

Our patent on QS-21 Stimulon composition of matter has expired and we rely primarily on unpatented technology and know-how to protect our rights to QS-21 Stimulon.

Our QS-21 Stimulon composition of matter patent family has expired, and our patent rights are limited to protecting certain combinations of QS-21 Stimulon with other adjuvants or formulations of QS-21 Stimulon with other agents, such as excipients that improve performance of the compound. However, there is no guarantee that a third party would necessarily choose to use QS-21 Stimulon in combination with such adjuvants or formulate it with the other agents covered by our patents. We are aware of other companies that claim to produce material comparable to QS-21 Stimulon. At least one other party has also developed derivatives of QS-21 that have shown biological activity.

S-20

Table of Contents

Although our licenses also rely on unpatented technology, know-how, and confidential information, these intellectual property rights may not be enforceable in certain jurisdictions, and we may not be able to collect anticipated revenue from our licensees. Any such inability would have a material adverse effect on our business, financial condition and results of operations.

We may become involved in lawsuits to protect or enforce our patents, which could be expensive, time consuming and unsuccessful.

Third parties may infringe or misappropriate our intellectual property, including our existing patents, patents that may issue to us in the future, or the patents of our licensors to which we have a license. As a result, we may be required to file infringement claims to stop third-party infringement or unauthorized use. Further, we may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

If we or one of our licensors were to initiate legal proceedings against a third party to enforce a patent covering our product candidates, the defendant could counterclaim that the patent covering our product candidates is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent.

In addition, within and outside of the United States, there has been a substantial amount of litigation and administrative proceedings, including interference and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in various foreign jurisdictions, regarding patent and other intellectual property rights in the biopharmaceutical industry. Recently, the AIA introduced new procedures, including inter partes review and post grant review. These procedures may be used by competitors to challenge the scope and/or validity of our patents, including those that patents perceived by our competitors as blocking entry into the market for their products, and the outcome of such challenges.

Even after they have been issued, our patents and any patents which we license may be challenged, narrowed, invalidated or circumvented. If our patents are invalidated or otherwise limited or will expire prior to the commercialization of our product candidates, other companies may be better able to develop products that compete with ours, which could adversely affect our competitive business position, business prospects and financial condition.

The following are examples of litigation and other adversarial proceedings or disputes that we could become a party to involving our patents or patents licensed to us:

- n we or our collaborators may initiate litigation or other proceedings against third parties to enforce our patent rights;
- n third parties may initiate litigation or other proceedings seeking to invalidate patents owned by or licensed to us or to obtain a declaratory judgment that their product or technology does not infringe our patents or patents licensed to us;

n

third parties may initiate opposition proceedings, post-grant review, inter partes review, or reexamination proceedings challenging the validity or scope of our patent rights, requiring us or our collaborators and/or licensors to participate in such proceedings to defend the validity and scope of our patents;

- n there may be a challenge or dispute regarding inventorship or ownership of patents currently identified as being owned by or licensed to us;
- n the USPTO may initiate an interference or derivation proceeding between patents or patent applications owned by or licensed to us and those of our competitors, requiring us or our collaborators and/or licensors to participate in an interference or derivation proceeding to determine the priority of invention, which could jeopardize our patent rights; or
- n third parties may seek approval to market biosimilar versions of our future approved products prior to expiration of relevant patents owned by or licensed to us, requiring us to defend our patents, including by filing lawsuits alleging patent infringement.

S-21

Table of Contents

These lawsuits and proceedings would be costly and could affect our results of operations and divert the attention of our managerial and scientific personnel. There is a risk that a court or administrative body could decide that our patents are invalid or not infringed by a third party's activities, or that the scope of certain issued claims must be further limited. An adverse outcome in a litigation or proceeding involving our own patents could limit our ability to assert our patents against these or other competitors, affect our ability to receive royalties or other licensing consideration from our licensees, and may curtail or preclude our ability to exclude third parties from making, using and selling similar or competitive products. An adverse outcome may also put our pending patent applications at risk of not issuing, or issuing with limited and potentially inadequate scope to cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. Additionally, it is also possible that prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, may, nonetheless, ultimately be found by a court of law or an administrative panel to affect the validity or enforceability of a claim, for example, if a priority claim is found to be improper. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we could lose at least part, and perhaps all, of the patent protection on our relevant product candidates. Such a loss of patent protection could have a material adverse impact on our business.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, during the course of litigation or administrative proceedings, there could be public announcements of the results of hearings, motions or other interim proceedings or developments or public access to related documents. If investors perceive these results to be negative, the market price for our common stock could be significantly harmed.

Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage. The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- n others may be able to develop a platform that is similar to, or better than, ours in a way that is not covered by the claims of our patents;
- n others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of our patents;
- n we might not have been the first to make the inventions covered by patents or pending patent applications;
- n we might not have been the first to file patent applications for these inventions;
- n

any patents that we obtain may not provide us with any competitive advantages or may ultimately be found invalid or unenforceable; or

n we may not develop additional proprietary technologies that are patentable.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our future approved products or impair our competitive position. In particular the patent landscape around the discovery, development, manufacture and commercial use of our six pre-clinical CPM antibody programs and therapeutic antibodies is crowded.

Third parties may have or obtain valid and enforceable patents or proprietary rights that could block us from developing product candidates using our technology. Our failure to obtain a license to any technology that we require may materially harm our business, financial condition and results of operations. Moreover, our failure to maintain a license to any technology that we require may also materially harm our business, financial condition, and results of operations. Furthermore, we would be exposed to a threat of litigation.

S-22

Table of Contents

In the biopharmaceutical industry, significant litigation and other proceedings regarding patents, patent applications, trademarks and other intellectual property rights have become commonplace. The types of situations in which we may become a party to such litigation or proceedings include:

- n we or our collaborators may initiate litigation or other proceedings against third parties seeking to invalidate the patents held by those third parties or to obtain a judgment that our products or processes do not infringe those third parties' patents;
- n if our competitors file patent applications that claim technology also claimed by us or our licensors, we or our licensors may be required to participate in interference, derivation or other proceedings to determine the priority of invention, which could jeopardize our patent rights and potentially provide a third party with a dominant patent position;
- n if third parties initiate litigation claiming that our processes or products infringe their patent or other intellectual property rights, we and our collaborators will need to defend against such proceedings; and
- n if a license to necessary technology is terminated, the licensor may initiate litigation claiming that our processes or products infringe or misappropriate their patent or other intellectual property rights and/or that we breached our obligations under the license agreement, and we and our collaborators would need to defend against such proceedings.

These lawsuits would be costly and could affect our results of operations and divert the attention of our management and scientific personnel. There is a risk that a court would decide that we or our collaborators are infringing the third party's patents and would order us or our collaborators to stop the activities covered by the patents. In that event, we or our collaborators may not have a viable alternative to the technology protected by the patent and may need to halt work on the affected product candidate or cease commercialization of an approved product. In addition, there is a risk that a court will order us or our collaborators to pay the other party damages. An adverse outcome in any litigation or other proceeding could subject us to significant liabilities to third parties and require us to cease using the technology that is at issue or to license the technology from third parties. We may not be able to obtain any required licenses on commercially acceptable terms or at all. Any of these outcomes could have a material adverse effect on our business.

The biopharmaceutical industry has produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform or predictable. If we are sued for patent infringement, we would need to demonstrate that our products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and divert management's time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid, we may incur substantial

monetary damages, encounter significant delays in bringing our product candidates to market and be precluded from manufacturing or selling our product candidates.

The cost of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the cost of such litigation and proceedings more effectively than we can because of their substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Patent litigation and other proceedings may also absorb significant management time.

S-23

Table of Contents

If we fail to comply with our obligations under our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are currently party to various intellectual property license agreements. These license agreements impose, and we expect that future license agreements may impose, various diligence, milestone payment, royalty, insurance and other obligations on us. These licenses typically include an obligation to pay an upfront payment, yearly maintenance payments and royalties on sales. If we fail to comply with our obligations under the licenses, the licensors may have the right to terminate their respective license agreements, in which event we might not be able to market any product that is covered by the agreements. Termination of the license agreements or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms, which could adversely affect our competitive business position and harm our business.

If we are unable to protect the confidentiality of our proprietary information, the value of our technology and products could be adversely affected.

In addition to patent protection, we also rely on other proprietary rights, including protection of trade secrets, and other proprietary information. To maintain the confidentiality of trade secrets and proprietary information, we enter into confidentiality agreements with our employees, consultants, collaborators and others upon the commencement of their relationships with us. These agreements require that all confidential information developed by the individual or made known to the individual by us during the course of the individual's relationship with us be kept confidential and not disclosed to third parties. Our agreements with employees and our personnel policies also provide that any inventions conceived by the individual in the course of rendering services to us shall be our exclusive property. However, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. Thus, despite such agreement, such inventions may become assigned to third parties. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. To the extent that our employees, consultants or contractors use technology or know-how owned by third parties in their work for us, disputes may arise between us and those third parties as to the rights in related inventions. To the extent that an individual who is not obligated to assign rights in intellectual property to us is rightfully an inventor of intellectual property, we may need to obtain an assignment or a license to that intellectual property from that individual, or a third party or from that individual's assignee. Such assignment or license may not be available on commercially reasonable terms or at all.

Adequate remedies may not exist in the event of unauthorized use or disclosure of our proprietary information. The disclosure of our trade secrets would impair our competitive position and may materially harm our business, financial condition and results of operations. Costly and time consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to maintain trade secret protection could adversely affect our competitive business position. In addition, others may independently discover or develop our trade secrets and proprietary information, and the existence of our own trade secrets affords no protection against such independent discovery.

As is common in the biopharmaceutical industry, we employ individuals who were previously or concurrently employed at research institutions and/or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, or we, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers, or that patents and applications we have filed to protect inventions of these employees, even those related to one or more of our product candidates, are rightfully owned by their former or concurrent employer. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial

costs and be a distraction to management.

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to the USPTO and various foreign patent offices at various points over the lifetime of our patents and/or applications. We have systems in place to remind us to pay these fees, and we rely on our outside counsel or service providers to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the

S-24

Table of Contents

patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business. In addition, we are responsible for the payment of patent fees for patent rights that we have licensed from other parties. If any licensor of these patents does not itself elect to make these payments, and we fail to do so, we may be liable to the licensor for any costs and consequences of any resulting loss of patent rights.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

Obtaining and enforcing patents in the pharmaceutical industry involves both technological and legal complexity, and therefore, is costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation. Further, recent U.S. Supreme Court rulings have either narrowed the scope of patent protection available in certain circumstances or weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained.

For our U.S. patent applications containing a claim not entitled to priority before March 16, 2013, there is a greater level of uncertainty in the patent law. In September 2011, the Leahy-Smith America Invents Act, or the American Invents Act, or AIA, was signed into law. The AIA includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The USPTO is currently developing regulations and procedures to govern administration of the AIA, and many of the substantive changes to patent law associated with the AIA. It is not clear what other, if any, impact the AIA will have on the operation of our business. Moreover, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a first-to-file system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application. Furthermore, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our technology and the prior art allow our technology to be patentable over the prior art. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our patents or patent applications.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal court necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court

action.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We may have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise improperly used or disclosed confidential information of these third parties or our employees' former employers. Further, we may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others

S-25

Table of Contents

who are involved in developing our product candidates. We may also be subject to claims that former employees, consultants, independent contractors, collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging our right to and use of confidential and proprietary information. If we fail in defending any such claims, in addition to paying monetary damages, we may lose our rights therein. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly developing countries. For example, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement on infringing activities is inadequate. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. In addition, certain countries in Europe and certain developing countries, including India and China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we may have limited remedies if our patents are infringed or if we are compelled to grant a license to our patents to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license. Finally, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

Risks Related to Litigation

We may face litigation or regulatory investigations that could result in substantial damages and may divert management's time and attention from our business.

From time to time we may become a party to legal proceedings, claims and investigations that arise in the ordinary course of business such as, but not limited to, patent, employment, commercial and environmental matters. While we currently believe that the ultimate outcome of any of these proceedings will not have a material adverse effect on our financial position, results of operations, or liquidity, litigation is subject to inherent uncertainty. Furthermore, litigation consumes both cash and management attention.

We maintain property and general commercial insurance coverage as well as errors and omissions and directors and officers insurance policies. This insurance coverage may not be sufficient to cover us for future claims.

We are also exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional and/or negligent failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with federal and state health care fraud and abuse, transparency, and/or data privacy and security laws and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in

S-26

Table of Contents

the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices; to promote transparency; and to protect the privacy and security of patient data. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements.

While we have adopted a corporate compliance program, we may not be able to protect against all potential issues of noncompliance. Efforts to ensure that our business complies with all applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law involving applicable laws and regulations.

Employee misconduct could also involve the improper use or disclosure of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. In addition, during the course of our operations, our directors, executives and employees may have access to material, nonpublic information regarding our business, our results of operations or potential transactions we are considering. We may not be able to prevent a director, executive or employee from trading in our common stock on the basis of, or while having access to, material, nonpublic information. If a director, executive or employee was to be investigated, or an action was to be brought against a director, executive or employee for insider trading, it could have a negative impact on our reputation and our stock price. Such a claim, with or without merit, could also result in substantial expenditures of time and money, and divert attention of our management team.

Product liability and other claims against us may reduce demand for our products and/or result in substantial damages.

We face an inherent risk of product liability exposure related to testing our product candidates in human clinical trials and may face even greater risks if we sell Oncophage® in Russia or our other product candidates commercially. An individual may bring a product liability claim against us if one of our product candidates causes, or merely appears to have caused, an injury. Product liability claims may result in:

- n decreased demand for our product candidates;
- n regulatory investigations;
- n injury to our reputation;
- n withdrawal of clinical trial volunteers;
- n costs of related litigation; and
- n substantial monetary awards to plaintiffs.

We manufacture the Prophage Series vaccines from a patient's cancer cells, and medical professionals must inject the vaccines into the same patient from which they were manufactured. A patient may sue us if a hospital, a shipping

company, or we fail to receive the removed cancer tissue or deliver that patient's vaccine. We anticipate that the logistics of shipping will become more complex if the number of patients we treat increases and that shipments of tumor and/or vaccines may be lost, delayed, or damaged. Additionally, complexities unique to the logistics of commercial products may delay shipments and limit our ability to move commercial product in an efficient manner without incident. We do not have any other insurance that covers loss of or damage to the Prophage Series vaccines or tumor material, and we do not know whether such insurance will be available to us at a reasonable price or at all. We have limited product liability coverage for use of our product candidates. Our product liability policy provides \$10.0 million aggregate coverage and \$10.0 million per occurrence coverage. This limited insurance coverage may be insufficient to fully cover us for future claims.

We are also subject to laws generally applicable to businesses, including but not limited to, federal, state and local wage and hour, employee classification, mandatory healthcare benefits, unlawful workplace discrimination and whistle-blowing. Any actual or alleged failure to comply with any regulation applicable to our business or any whistle-blowing claim, even if without merit, could result in costly litigation, regulatory action or otherwise harm our business, results of operations, financial condition, cash flow and future prospects.

S-27

Table of Contents

If we do not comply with environmental laws and regulations, we may incur significant costs and potential disruption to our business.

We use or may use hazardous, infectious, and radioactive materials, and recombinant DNA in our operations, which have the potential of being harmful to human health and safety or the environment. We store these hazardous (flammable, corrosive, toxic), infectious, and radioactive materials, and various wastes resulting from their use, at our facilities pending use and ultimate disposal. We are subject to a variety of federal, state, and local laws and regulations governing use, generation, storage, handling, and disposal of these materials. We may incur significant costs complying with both current and future environmental health and safety laws and regulations. In particular, we are subject to regulation by the Occupational Safety and Health Administration, the Environmental Protection Agency, the Drug Enforcement Agency, the Department of Transportation, the Centers for Disease Control and Prevention, the National Institutes of Health, the International Air Transportation Association, and various state and local agencies. At any time, one or more of the aforementioned agencies could adopt regulations that may affect our operations. We are also subject to regulation under the Toxic Substances Control Act and the Resource Conservation Development programs.

Although we believe that our current procedures and programs for handling, storage, and disposal of these materials comply with federal, state, and local laws and regulations, we cannot eliminate the risk of accidents involving contamination from these materials. Although we have a workers' compensation liability policy, we could be held liable for resulting damages in the event of an accident or accidental release, and such damages could be substantially in excess of any available insurance coverage and could substantially disrupt our business.

Risks Related to our Common Stock

Provisions in our organizational documents could prevent or frustrate attempts by stockholders to replace our current management.

Our certificate of incorporation and bylaws contain provisions that could make it more difficult for a third party to acquire us without the consent of our Board of Directors. Our certificate of incorporation provides for a staggered board and removal of directors only for cause. Accordingly, stockholders may elect only a minority of our Board at any annual meeting, which may have the effect of delaying or preventing changes in management. In addition, under our certificate of incorporation, our Board of Directors may issue additional shares of preferred stock and determine the terms of those shares of stock without any further action by our stockholders. Our issuance of additional preferred stock could make it more difficult for a third party to acquire a majority of our outstanding voting stock and thereby effect a change in the composition of our Board of Directors. Our certificate of incorporation also provides that our stockholders may not take action by written consent. Our bylaws require advance notice of stockholder proposals and director nominations and permit only our president or a majority of the Board of Directors to call a special stockholder meeting. These provisions may have the effect of preventing or hindering attempts by our stockholders to replace our current management. In addition, Delaware law prohibits a corporation from engaging in a business combination with any holder of 15% or more of its capital stock until the holder has held the stock for three years unless, among other possibilities, the board of directors approves the transaction. Our Board of Directors may use this provision to prevent changes in our management. Also, under applicable Delaware law, our Board of Directors may adopt additional anti-takeover measures in the future.

The first right to negotiate provision contained in our agreement with one of our licensees could hinder or delay a change of control of our company or the sale of certain of our assets.

We have entered into a First Right to Negotiate and Amendment Agreement with GSK that affords GSK, one of our licensees, a first right to negotiate with us in the event we determine to initiate a process to effect a change of control of our company with, or to sell certain of our assets to, an unaffiliated third party or in the event that a third party commences an unsolicited tender offer seeking a change of control of our company. In such event, we must provide GSK a period of time to determine whether it wishes to negotiate the terms of such a transaction with us. If GSK affirmatively so elects, we are required to negotiate with GSK in good faith towards effecting a transaction of that nature for a specified period. During the negotiation period, we are obligated not to enter into a definitive agreement with a third party that would preclude us from negotiating and/or executing a definitive agreement with GSK. If GSK determines not to negotiate with us or we are unable to come to an agreement with GSK during this period, we may enter into the specified change of control or sale transaction within the following 12 months, provided that such a transaction is not on terms in the aggregate that are materially less favorable to us and our

S-28

Table of Contents

stockholders (as determined by our Board of Directors, in its reasonable discretion) than terms last offered to us by GSK in a binding written proposal during the negotiation period. The first right to negotiate terminates on March 2, 2017. Although GSK's first right to negotiate does not compel us to enter into a transaction with GSK nor prevent us from negotiating with or entering into a transaction with a third party, the first right to negotiate could inhibit a third party from engaging in discussions with us concerning such a transaction or delay our ability to effect such a transaction with a third party.

Our stock has historically had low trading volume, and its public trading price has been volatile.

For the period from our initial public offering on February 4, 2000 to March 31, 2015, and for the three months ended March 31, 2015, the closing price of our common stock has fluctuated between \$1.80 (or \$0.30 pre-reverse stock split) and \$315.78 (or \$52.63 pre-reverse stock split) per share and \$3.91 and \$6.17 per share, respectively. The average daily trading volume for the three months ended March 31, 2015 was approximately 2,176,000 shares while the average daily trading volume for the year ended December 31, 2014 was approximately 728,000. The market may experience significant price and volume fluctuations that are often unrelated to the operating performance of individual companies. In addition to general market volatility, many factors may have a significant adverse effect on the market price of our stock, including:

- n continuing operating losses, which we expect over the next several years as we continue our development activities;
- n announcements of decisions made by public officials;
- n results of our pre-clinical studies and clinical trials;
- n announcements of new collaboration agreements with strategic partners or developments by our existing collaborative partners;
- n announcements of acquisitions;
- n announcements of technological innovations, new commercial products, failures of products, or progress toward commercialization by our competitors or peers;
- n failure to realize the anticipated benefits of acquisitions, including our acquisition of 4-AB and certain assets from Celexion, LLC;
- n developments concerning proprietary rights, including patent and litigation matters;

- n publicity regarding actual or potential results with respect to product candidates under development;
- n quarterly fluctuations in our financial results;
- n variations in the level of expenses related to any of our product candidates or clinical development programs;
- n additions or departures of key management or scientific personnel;
- n conditions or trends in the biotechnology and biopharmaceutical industries;
- n other events or factors, including those resulting from war, incidents of terrorism, natural disasters or responses to these events;
- n changes in accounting principles;
- n general economic and market conditions and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies; and
- n sales of common stock by us or our stockholders in the future, as well as the overall trading volume of our common stock.

In the past, securities class action litigation has often been brought against a company following a significant decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies generally experience significant stock price volatility.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who covers us downgrades our stock, or publishes inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, demand for our stock could decrease, which could cause our stock price and trading volume to decline.

Table of Contents

The sale of a significant number of shares could cause the market price of our stock to decline.

The sale by us or the resale by stockholders of a significant number of shares of our common stock could cause the market price of our common stock to decline. As of April 30, 2015, we had 71,507,832 shares of common stock outstanding. All of these shares are eligible for sale on Nasdaq, although certain of the shares are subject to sales volume and other limitations. As of the date hereof, we had filed registration statements to permit the sale of approximately 12,200,000 shares of common stock under our equity incentive plans. We have also filed registration statements to permit the sale of approximately 167,000 shares of common stock under our employee stock purchase plan, to permit the sale of 225,000 shares of common stock under our Directors' Deferred Compensation Plan, to permit the sale of approximately 8,274,000 shares of common stock pursuant to various private placement agreements and to permit the sale of approximately 10,000,000 shares of our common stock pursuant to our At Market Issuance Sales Agreement. As of March 31, 2015, an aggregate of approximately 22.0 million of these shares remain available for sale. Contingent milestone payments, payable in cash or shares of our common stock at our option, will be due to the former shareholders of 4-AB as follows (i) \$10 million upon our market capitalization exceeding \$750 million for 30 consecutive trading days prior to the earliest of (a) the tenth anniversary of the Closing Date (b) the sale of 4-AB or (c) the sale of Agenesis and (ii) \$10 million upon our market capitalization exceeding \$1.0 billion for 30 consecutive trading days prior to the earliest of (a) the tenth anniversary of the Closing Date, (b) the sale of 4-AB or (c) the sale of Agenesis. In addition, as additional consideration for purchased assets, we agreed to pay to Celexion \$4.0 million on each of the 12-month and 24-month anniversaries of the Closing Date payable at our discretion in cash, shares of our common stock, or any combination thereof. We intend to file one or more registration statements covering the resale of shares of our common stock held by certain of our stockholders or investors in 2015. We are also obligated to file registration statements covering any additional shares that may be issued to Celexion in the future pursuant to the terms of our agreement with Celexion.

As of April 30, 2015, warrants to purchase approximately 4,351,450 shares of our common stock with a weighted average exercise price per share of \$9.01 were outstanding.

As of April 30, 2015, options to purchase 7,692,759 shares of our common stock with a weighted average exercise price per share of \$4.52 were outstanding. These options are subject to vesting that occurs over a period of up to four years following the date of grant. As of April 30, 2015 we had 66,328 nonvested shares outstanding.

As of April 30, 2015, our outstanding shares of Series A-1 Convertible Preferred Stock were convertible into 333,333 shares of our common stock.

We may issue additional common stock, preferred stock, restricted stock units, or securities convertible into or exchangeable for our common stock. Furthermore, substantially all shares of common stock for which our outstanding stock options or warrants are exercisable are, once they have been purchased, eligible for immediate sale in the public market. The issuance of additional common stock, preferred stock, restricted stock units, or securities convertible into or exchangeable for our common stock or the exercise of stock options or warrants would dilute existing investors and could adversely affect the price of our securities. In addition, such securities may have rights senior to the rights of securities held by existing investors.

We do not intend to pay dividends on our common stock and, consequently your ability to obtain a return on your investment will depend on appreciation in the price of our common stock.

We have never declared or paid any cash dividend on our common stock and do not intend to do so in the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business. Therefore, the success of an investment in shares of our common stock will depend upon any future

appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or maintain their current value.

S-30

Table of Contents

Failure to maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act of 2002 and to comply with changing regulation of corporate governance and public disclosure could have a material adverse effect on our operating results and the price of our common stock.

The Sarbanes-Oxley Act of 2002 and rules adopted by the SEC and Nasdaq have resulted in significant costs to us. In particular, our efforts to comply with Section 404 of the Sarbanes-Oxley Act of 2002 and related regulations regarding the required assessment of our internal control over financial reporting, and our independent registered public accounting firm's audit of internal control over financial reporting, have required commitments of significant management time. We expect these commitments to continue.

Our internal control over financial reporting (as defined in Rules 13a-15 of the Exchange Act) is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our consolidated financial statements for external purposes in accordance with U.S. GAAP. Because of its inherent limitations, internal control over financial reporting may not prevent or detect all deficiencies or weaknesses in our financial reporting. While our management has concluded that there were no material weaknesses in our internal control over financial reporting as of December 31, 2014, our procedures are subject to the risk that our controls may become inadequate because of changes in conditions or as a result of a deterioration in compliance with such procedures. No assurance is given that our procedures and processes for detecting weaknesses in our internal control over financial reporting will be effective.

We anticipate additional commitments of management time to ensure that our internal control over financial reporting of the operations of 4-AB complies with Section 404 of the Sarbanes-Oxley Act of 2002. Prior to the acquisition, 4-AB was a privately held company organized under the laws of Switzerland and, as such, it had not been subject to financial reporting requirements applicable to public companies and was not required to prepare and publish audited financial statements in accordance with U.S. GAAP. Accordingly, our on-going efforts to ensure that our internal control over the financial reporting of the operations of 4-AB will cause us to incur significant additional costs.

Changing laws, regulations and standards relating to corporate governance and public disclosure, are creating uncertainty for companies. Laws, regulations and standards are subject to varying interpretations in some cases due to their lack of specificity, and as a result, their application in practice may evolve over time as new guidance is provided, which could result in continuing uncertainty regarding compliance matters and higher costs caused by ongoing revisions to disclosure and governance practices. If we fail to comply with these laws, regulations and standards, our reputation may be harmed and we might be subject to sanctions or investigation by regulatory authorities, such as the SEC. Any such action could adversely affect our operating results and the market price of our common stock.

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds to us from this offering, after deduction of underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately \$ million (or approximately \$ if the underwriters' option to purchase additional shares is exercised in full).

We intend to use the net proceeds from this offering to fund our continued research and development initiatives in connection with expanding our product pipeline and for other general corporate purposes, which may include working capital, capital expenditures, clinical trial expenditures, acquisitions of additional companies or technologies and investments.

The timing and amounts of our actual expenditures will depend on several factors, including data results, progression of our pre-clinical programs as well as our joint collaborators. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. Accordingly, our management will have broad discretion in the application of these proceeds. Pending the uses described above, we will invest the net proceeds in short-term, investment-grade, interest-bearing instruments in accordance with our investment policy.

S-32

Table of Contents**DILUTION**

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share and the pro forma net tangible book value per share after this offering. We calculate net tangible book value per share by dividing the net tangible book value, which represents total assets less goodwill and intangible assets reduced by total liabilities, by the number of outstanding shares of our common stock.

Our net tangible book value as of March 31, 2015 was approximately \$21.2 million, or \$0.30 per share. After giving effect to the sale by us of shares of common stock in this offering at a public offering price of \$ per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma net tangible book value as of March 31, 2015 would have been approximately \$ million, or \$ per share. This represents an immediate increase in pro forma net tangible book value of \$ per share to existing stockholders and an immediate dilution of \$ per share to new investors purchasing our common stock in this offering.

The following table illustrates this dilution on a per share basis:

Public offering price per share	\$
Net tangible book value per share as of March 31, 2015	\$ 0.30
Increase in net tangible book value per share after this offering	\$
Pro forma net tangible book value per share as of March 31, 2015, after giving effect to this offering	\$
Dilution per share to new investors in this offering	\$

The information above assumes that the underwriters do not exercise their option to purchase additional shares. If the underwriters exercise their option to purchase additional shares in full, our net tangible book value per share after giving effect to this offering would be \$ per share, and the dilution in net tangible book value per share to investors in this offering would be \$ per share.

The above discussion and table are based on 70,836,180 shares of our common stock outstanding as of March 31, 2015 and does not reflect:

the impact of our acquisition of certain assets from Celexion, LLC, or Celexion, on April 7, 2015, pursuant to the terms of our Asset Purchase Agreement dated April 7, 2015 among us, Celexion and its members, or the Celexion Purchase Agreement, including without limitation the 574,140 shares that we issued to Celexion on April 7, 2015, the \$1.0 million that we paid to Celexion on April 7, 2015, and the additional consideration payable to Celexion pursuant to the terms of the Celexion Purchase Agreement;

- n 4,351,450 shares issuable upon the exercise of outstanding warrants with a weighted-average exercise price of \$9.01 per share;
- n 7,834,555 shares issuable upon the exercise of outstanding stock options with a weighted-average exercise price of \$4.56 per share;
- n 67,578 nonvested shares;
- n 333,333 shares issuable upon the conversion of our outstanding shares of Series A-1 Convertible Preferred Stock;
- n 167,000 shares available under our Employee Stock Purchase Plan;
- n 174,224 shares issuable under our Directors' Deferred Compensation Plan; and
- n 809,370 shares reserved for future issuance under our 2009 Plan, or an additional 4,000,000 shares reserved for future issuance under our 2009 Plan for which our board of directors approved an increase in March 2015, subject to approval by our stockholders at our 2015 annual meeting of stockholders.

Table of Contents

On April 30, 2015, there were 71,507,832 shares of our common stock outstanding not including:

- n 4,351,450 shares issuable upon the exercise of outstanding warrants with a weighted-average exercise price of \$9.01 per share;
- n 7,692,759 shares issuable upon the exercise of outstanding stock options with a weighted-average exercise price of \$4.52 per share;
- n 66,328 nonvested shares;
- n 333,333 shares issuable upon the conversion of our outstanding shares of Series A-1 Convertible Preferred Stock;
- n 167,000 shares available under our Employee Stock Purchase Plan;
- n 174,224 shares issuable under our Directors' Deferred Compensation Plan; and
- n 839,376 shares reserved for future issuance under our 2009 Plan, or an additional 4,000,000 shares reserved for future issuance under our 2009 Plan for which our board of directors approved an increase in March 2015, subject to approval by our stockholders at our 2015 annual meeting of stockholders.

Table of Contents

MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following is a general discussion of the material U.S. federal income and estate tax considerations applicable to non-U.S. holders with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. All prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock. In general, a non-U.S. holder means a beneficial owner of our common stock (other than a partnership or an entity or arrangement treated as a partnership for U.S. federal income tax purposes) that is not, for U.S. federal income tax purposes:

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

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing U.S. Treasury Regulations promulgated thereunder, published administrative rulings and judicial decisions, all as in effect as of the date of this prospectus. These laws are subject to change and to differing interpretation, possibly with retroactive effect. Any change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus.

We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, held for investment). This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances, nor does it address any aspects of U.S. state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as holders that own, or are deemed to own, more than 5% of our capital stock (except to the extent specifically set forth below), corporations that accumulate earnings to avoid U.S. federal income tax, tax-exempt organizations, banks, financial institutions, insurance companies, real estate investment trusts, brokers, dealers or traders in securities, commodities or currencies, tax-qualified retirement plans, holders subject to the alternative minimum tax or the Medicare contribution tax, holders who hold or receive our common stock pursuant to the exercise of employee stock options or otherwise as compensation, holders holding our common stock as part of a hedge, straddle or other risk reduction strategy, conversion transaction or other integrated investment, holders deemed to sell our common stock under the constructive sale provisions of the Code, controlled foreign corporations, passive foreign investment companies and certain former U.S. citizens or long-term residents.

In addition, this discussion does not address the tax treatment of partnerships (or entities or arrangements that are treated as partnerships for U.S. federal income tax purposes) or persons that hold their common stock through such partnerships. If a partnership, including any entity or arrangement treated as a partnership for U.S. federal income tax purposes, holds shares of our common stock, the U.S. federal income tax treatment of a partner in such partnership will generally depend upon the status of the partner and the activities of the partnership. Such partners and partnerships should consult their tax advisors regarding the tax consequences of the purchase, ownership and disposition of our common stock.

There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein, and we have not obtained, nor do we intend to obtain, a ruling with respect to the U.S. federal income or estate tax consequences to a non-U.S. holder of the purchase, ownership or disposition of our common stock.

S-35

Table of Contents

Distributions on Our Common Stock

Distributions, if any, on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's adjusted tax basis in the common stock. Any remaining excess will be treated as capital gain from the sale or exchange of such common stock, subject to the tax treatment described below in **Gain on Sale, Exchange or Other Disposition of Our Common Stock**. Any such distribution will also be subject to the discussion below under the heading **Foreign Accounts**.

Dividends paid to a non-U.S. holder will generally 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 between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, 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 between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS.

Gain on Sale, Exchange or Other Disposition of Our Common Stock

Subject to the discussion below regarding backup withholding and foreign accounts, in general, a non-U.S. holder will not be subject to any U.S. federal income tax on any gain realized upon such holder's sale, exchange or other disposition of shares of our common stock unless:

- n the gain is effectively connected with a U.S. trade or business of the non-U.S. holder and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed base maintained in the United States by such non-U.S. holder, in which case the non-U.S. holder generally will be taxed at the graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in **Distributions on Our Common Stock** also may apply;

- n the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty) on the net gain derived from the disposition, which may be offset by U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States) provided the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or
- n our common stock constitutes a U.S. real property interest because we are, or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a U.S. real property holding corporation. Even if we are or become a U.S. real property holding corporation, provided that our common stock is regularly traded on an established securities market, our common stock will be treated as a U.S. real property interest only with respect to a non-U.S. holder that holds more than

S-36

Table of Contents

5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. In such case, such non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. 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. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will continue to be regularly traded on an established securities market for purposes of the rules described above.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the dividends on our common stock paid to such holder and the tax withheld, if any, with respect to such dividends. Non-U.S. holders will have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to the U.S. withholding tax, as described above in *Distributions on Our Common Stock*, generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

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

Foreign Accounts

The Foreign Account Tax Compliance Act provisions of the Hiring Incentives to Restore Employment Act, or FATCA, generally imposes a U.S. federal withholding tax of 30% on dividends and the gross proceeds of a disposition of our common stock paid to a foreign financial institution (as specifically defined for this purpose), unless such institution enters into an agreement with the U.S. government to, among other things, withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners). A U.S. federal withholding tax of 30% also applies to dividends and the gross proceeds of a disposition of our common stock paid to a non-financial foreign entity, as specifically defined for this purpose, unless such entity provides the withholding agent with either a certification that it does not

have any substantial direct or indirect U.S. owners or provides information regarding substantial direct and indirect U.S. owners of the entity. The withholding provisions described above currently apply to dividends paid on our common stock and will generally apply with respect to gross proceeds of a sale or other disposition of our common stock on or after January 1, 2017. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph.

S-37

Table of Contents

U.S. Federal Estate Tax

Shares of our common stock that are owned or treated as owned at the time of death by an individual who is not a citizen or resident of the United States, as specifically defined for U.S. federal estate tax purposes, are considered U.S. situs assets and will be included in the individual's gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE PARTICULAR U.S. FEDERAL, STATE AND LOCAL AND NON-U.S. TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGES IN APPLICABLE LAWS.

S-38

Table of Contents**UNDERWRITING**

Subject to the terms and conditions set forth in the underwriting agreement, dated _____, 2015, among us and Jefferies LLC and William Blair & Company, L.L.C., as the representatives of the underwriters named below and the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

UNDERWRITER	NUMBER OF SHARES
Jefferies LLC	
William Blair & Company, L.L.C.	
Oppenheimer & Co. Inc.	
Total	

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them 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 and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not intend to confirm sales to any account over which they exercise discretionary authority.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$ per share of common stock. After the offering, the public offering price, concession and reallowance to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

S-39

Table of Contents

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	PER SHARE		TOTAL	
	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES	WITH OPTION TO PURCHASE ADDITIONAL SHARES	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES	WITH OPTION TO PURCHASE ADDITIONAL SHARES
Public offering price	\$	\$	\$	\$
Underwriting discounts and commissions paid by us	\$	\$	\$	\$
Proceeds to us, before expenses	\$	\$	\$	\$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$.

Listing

Our common stock is listed on the Nasdaq Capital Market under the trading symbol AGEN .

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to additional shares of our common stock from us at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above.

No Sales of Similar Securities

We and each of our executive officers and directors have agreed, subject to specified exceptions, not to directly or indirectly:

sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open put equivalent position within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended, or

- n otherwise dispose of any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially, or

- n publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus supplement without the prior written consent of Jefferies LLC.

These restrictions terminate after the close of trading of the common stock on and including the 90th day after the date of this prospectus supplement. However, subject to certain exceptions, in the event that either:

- n during the last 17 days of the 90 day restricted period, we issue an earnings release or material news or a material event relating to us occurs, or

- n prior to the expiration of the 90 day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90 day restricted period, then in either case the expiration of the 90 day restricted period will be extended until the expiration of the 18-day period beginning on the date of the issuance of an earnings release or the occurrence of the material news or event, as applicable, unless Jefferies LLC waives, in writing, such an extension.

Jefferies LLC may, in its sole discretion and at any time or from time to time before the termination of the 90 day restricted period release all or any portion of the securities subject to lock-up agreements. There are no existing

Table of Contents

agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either covered short sales or naked short sales.

Covered short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock 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 to purchase additional shares.

Naked short sales are sales in excess of the option to purchase additional shares of our common stock. 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 the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. 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. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member is purchased in a syndicate covering transaction and therefore has not been effectively placed by such syndicate member.

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. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on the Nasdaq Capital Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

This prospectus supplement and the accompanying prospectus in electronic format may be made available by e-mail or on the websites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than this prospectus supplement and the accompanying prospectus in electronic format, the information on the underwriters' websites and any information contained in any other website maintained by any of the underwriters is not part of this prospectus supplement or the accompanying prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

S-41

Table of Contents

Other Activities and 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. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of 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, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Disclaimers About Non-U.S. Jurisdictions

Australia

This prospectus supplement and the accompanying prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus supplement and the accompanying prospectus in Australia:

You confirm and warrant that you are either:

- n a sophisticated investor under section 708(8)(a) or (b) of the Corporations Act;
- n a sophisticated investor under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
- n a person associated with the company under Section 708(12) of the Corporations Act; or
- n a professional investor within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this prospectus supplement and the accompanying prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus supplement and the accompanying prospectus for resale in Australia within 12 months of those shares being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

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

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

S-42

Table of Contents

(b) 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

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of securities 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 of securities to the public in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, 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.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong, or SFO, and any rules made under that Ordinance; or in other circumstances which do not result in the document being a prospectus as defined in the Companies Ordinance (Cap. 32) of Hong Kong, or CO, or which do not constitute an offer or invitation to the public for the purpose of the CO or the SFO. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors as defined in the SFO and any rules made under that Ordinance.

This prospectus supplement and the accompanying prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus supplement and the accompanying prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus supplement and the accompanying prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the underwriters will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan, except pursuant

to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus supplement and the accompanying prospectus has not been and will not be lodged or registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and the accompanying prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in

S-43

Table of Contents

Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares of common stock pursuant to an offer made under Section 275 of the SFA except:
 - (i) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
 - (ii) where no consideration is or will be given for the transfer;
 - (iii) where the transfer is by operation of law;
 - (iv) as specified in Section 276(7) of the SFA; or
 - (v) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus supplement and the accompanying prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus supplement and the accompanying prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus supplement, the accompanying prospectus nor any other offering or marketing material relating to the offering, the company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus supplement and the accompanying prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

United Kingdom

This prospectus supplement and the accompanying prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order, and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated, each such person being referred to as a relevant person.

This prospectus supplement and the accompanying prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

S-44

Table of Contents

DESCRIPTION OF COMMON STOCK

In this offering, we are offering shares of common stock. The material terms and provisions of our common stock are described under the caption Description of Common Stock starting on page 12 of the accompanying prospectus.

S-45

Table of Contents

LEGAL MATTERS

Choate, Hall & Stewart LLP, Boston, Massachusetts, will pass on the validity of the shares of common stock offered by this prospectus supplement. Cooley LLP, New York, New York, is counsel for the underwriters in connection with this offering.

S-46

Table of Contents

EXPERTS

The consolidated financial statements of Agenus Inc. as of December 31, 2014 and 2013, and for each of the years in the three-year period ended December 31, 2014, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2014 have been incorporated by reference herein and in the registration statement in reliance upon the reports of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing. The audit report on the effectiveness of internal control over financial reporting as of December 31, 2014 contains an explanatory paragraph that states Agenus Inc. acquired 4-Antibody AG during 2014, and management excluded from its assessment of the effectiveness of Agenus Inc. and subsidiaries' internal control over financial reporting as of December 31, 2014 4-Antibody AG's internal control over financial reporting associated with total assets of approximately \$4.2 million and revenue of \$1.5 million that was included in Agenus Inc.'s consolidated financial statements as of and for the year ended December 31, 2014. The audit of internal control over financial reporting of Agenus Inc. and subsidiaries also excluded an evaluation of the internal control over financial reporting of 4-Antibody AG.

S-47

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. These documents are on file with the SEC under file number 000-29089. You may read and copy any document we file 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. In addition, we file many of our documents electronically with the SEC, and you may access those documents over the Internet. The SEC maintains a web site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. The address of the SEC's website is <http://www.sec.gov>. Documents we have filed with the SEC are also available on our website at www.agenusbio.com. The contents of our website are not part of, or incorporated into, this prospectus supplement or the accompanying prospectus. Our stock is quoted on the Nasdaq Capital Market under the symbol AGEN.

S-48

Table of Contents

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

This prospectus supplement and the accompanying prospectus are part of a registration statement on Form S-3 filed by us with the SEC. This prospectus supplement and the accompanying prospectus do not contain all of the information set forth in the registration statement, certain parts of which are omitted in accordance with the rules and regulations of the SEC. Statements contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference into this prospectus supplement or the accompanying prospectus as to the contents of any contract or other document referred to are not necessarily complete and in each instance reference is made to the copy of that contract or other document filed with the SEC. For further information about us and the securities offered by this prospectus supplement, we refer you to the registration statement and its exhibits and schedules which may be obtained as described herein.

The SEC allows us to incorporate by reference the information contained in documents that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and information in documents that we file later with the SEC will automatically update and supersede information in this prospectus supplement and the accompanying prospectus. We incorporate by reference the documents listed below into this prospectus supplement, and any future filings made by us with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act until the offering of all the securities by this prospectus supplement is completed, including all filings made after the date of this prospectus supplement. We hereby incorporate by reference the documents listed below (File No. 000-29089).

- n our Annual Report on Form 10-K for the fiscal year ended December 31, 2014 as filed on March 16, 2015;
- n our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2015 as filed on May 1, 2015;
- n our Current Reports on Form 8-K as filed on May 14, 2015, April 28, 2015, April 24, 2015, April 8, 2015, February 26, 2015, February 19, 2015 and January 9, 2015 (except, with respect to each of the foregoing, for portions of such reports which were deemed to be furnished and not filed);
- n our Proxy Statement on Schedule 14A filed with the SEC on April 30, 2015; and
- n the description of our common stock contained in our registration statement on Form 8-A filed under the Securities Exchange Act on January 24, 2000, including any amendment or reports filed for the purpose of updating such descriptions.

We will provide to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, at no cost to the requester, a copy of any and all of the information that is incorporated by reference in this prospectus.

Requests for such documents should be directed to:

Agenus Inc.

Edgar Filing: AGENUS INC - Form 424B5

3 Forbes Road

Lexington, MA 02421

Attention: Legal Department

Telephone: (781) 674-4400

S-49

Table of Contents

PROSPECTUS

\$150,000,000

of

Common Stock

Preferred Stock

Warrants

Debt Securities

Units

We may offer to sell to the public, from time to time in one or more offerings for an aggregate initial offering price of up to \$150,000,000:

shares of our common stock;

shares of our preferred stock;

warrants to purchase shares of our common stock, preferred stock and/or debt securities;

debt securities consisting of debentures, notes, or other evidences of indebtedness; or

units consisting of any combination of the foregoing securities.

We may offer and sell any combination of the securities in amounts, at prices and on terms that we will determine at the time of any particular offering, to or through one or more agents, dealers or underwriters, or directly to purchasers, including through subscription rights offerings, on a continuous or delayed basis. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement.

This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus. The prospectus

supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any applicable prospectus supplement before you invest.

Our common stock is listed on The NASDAQ Capital Market and trades under the symbol AGEN. On October 8, 2014, the last sale price of our common stock as reported on the NASDAQ Capital Market was \$2.81 per share. The other securities that may be offered are not listed on any securities exchange or included in any automated quotation system.

Investing in our securities involves risks. See Risk Factors on page 4 of this prospectus.

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

The date of this prospectus is October 23, 2014.

Table of Contents

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	Page 1
<u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>	2
<u>CAUTIONARY NOTE ABOUT FORWARD-LOOKING STATEMENTS</u>	3
<u>RISK FACTORS</u>	4
<u>THE COMPANY</u>	5
<u>USE OF PROCEEDS</u>	7
<u>RATIO OF EARNINGS TO FIXED CHARGES</u>	8
<u>DILUTION</u>	9
<u>DESCRIPTION OF SECURITIES</u>	10
<u>DESCRIPTION OF CAPITAL STOCK</u>	11
<u>DESCRIPTION OF COMMON STOCK</u>	12
<u>DESCRIPTION OF PREFERRED STOCK</u>	15
<u>DESCRIPTION OF WARRANTS</u>	17
<u>DESCRIPTION OF DEBT SECURITIES</u>	21
<u>DESCRIPTION OF UNITS</u>	28
<u>LEGAL OWNERSHIP AND BOOK-ENTRY ISSUANCE</u>	32
<u>PLAN OF DISTRIBUTION</u>	36
<u>LEGAL MATTERS</u>	38
<u>EXPERTS</u>	39
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	40

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission (the SEC), using a shelf registration process for the delayed offering and sale of securities pursuant to Rule 415 under the Securities Act of 1933, as amended (the Securities Act). Under the shelf process, we may, from time to time, sell any of the Securities described in this prospectus in one or more offerings for an aggregate initial offering price of up to \$150,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading **Where You Can Find More Information** beginning on page 40 of this prospectus.

We have not authorized anyone to provide you with any additional information. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

As used in this prospectus, unless the context otherwise requires, the terms **we**, **us**, **our**, **the Company** and **Agenus** mean, collectively, Agenus Inc. and its subsidiaries and their predecessors.

Table of Contents

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference in this prospectus the information we file with the SEC. This helps us disclose certain important information to you by referring you to the documents we file. The information we incorporate by reference is an important part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. We incorporate by reference each of the documents listed below.

our Annual Report on Form 10-K for the year ended December 31, 2013 (File No. 000-29089);

our Quarterly Report on Form 10-Q for the quarter ended June 30, 2014 (File No. 000-29089);

our Quarterly Report on Form 10-Q for the quarter ended March 31, 2014 (File No. 000-29089);

our Current Reports on Form 8-K filed on July 24, 2014, July 1, 2014, June 30, 2014, June 27, 2014, June 16, 2014, April 28, 2014, April 25, 2014, April 2, 2014, March 20, 2014, March 5, 2014, February 21, 2014, February 13, 2014 (as amended by our Current Report on Form 8-K/A filed on April 29, 2014), February 6, 2014, February 4, 2014, January 21, 2014, January 14, 2014 and January 13, 2014 (except, with respect to each of the foregoing, for portions of such reports which were deemed to be furnished and not filed) (File No. 000-29089);

our Proxy Statement on Schedule 14A filed with the SEC on March 10, 2014 (File No. 000-29089); and

the description of our common stock contained in our registration statement on Form 8-A filed under the Securities Exchange Act of 1934, as amended (the Exchange Act) on January 24, 2000, including any amendment or reports filed for the purpose of updating such descriptions (File No. 000-29089).

All filings by Agenus pursuant to the Exchange Act subsequent to the date hereof and prior to effectiveness of this registration statement are incorporated in this registration statement and deemed to be a part hereof from the date of filing of such documents or reports. In addition, all documents and reports filed by Agenus subsequent to the date hereof pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act prior to the filing of a post-effective amendment which indicates that all securities offered have been sold or which deregisters all securities remaining unsold, shall be deemed to be incorporated by reference in this registration statement and to be a part hereof from the date of filing of such documents or reports. Any statement contained in a document incorporated by reference herein shall be deemed to be modified or superseded to the extent that a statement contained herein or in any other subsequently filed document which also is incorporated by reference herein modifies or supersedes such statement. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements.

Edgar Filing: AGENUS INC - Form 424B5

You may obtain copies of these documents, other than exhibits, free of charge on the Company's website, www.agenusbio.com, as soon as reasonably practicable after they have been filed with the SEC and through the SEC's website, www.sec.gov.

- 2 -

Table of Contents

CAUTIONARY NOTE ABOUT FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement, and any information incorporated by reference into this prospectus or prospectus supplement may contain certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Exchange Act. You can identify these forward-looking statements by the fact they use words such as could, expect, anticipate, estimate, target, may, project, guidance, intention, will, potential, opportunity, future and other words and terms of similar meaning and expression in connection with any discussion of future operating or financial performance. You can also identify forward-looking statements by the fact that they do not relate strictly to historical or current facts. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes to differ materially from current expectations. These statements are likely to relate to, among other things, our business strategy, our research and development, our product development efforts, our ability to commercialize our product candidates, the activities of our licensees, our prospects for initiating partnerships or collaborations, the timing of the introduction of products, the effect of new accounting pronouncements, uncertainty regarding our future operating results and our profitability, anticipated sources of funds as well as our plans, objectives, expectations and intentions.

Although the Company believes it has been prudent in its plans and assumptions, no assurance can be given that any goal or plan set forth in forward-looking statements can be achieved and readers are cautioned not to place undue reliance on such statements, which speak only as of the date made. The Company undertakes no obligation to release publicly any revisions to forward-looking statements as a result of new information, future events or otherwise.

Retrocyte Display® and Stimulon® are registered trademarks of Agenus Inc. and its subsidiaries. All rights reserved.

Table of Contents

RISK FACTORS

Before purchasing any of the securities you should carefully consider the risk factors relating to Agenus incorporated by reference in this prospectus from our Quarterly Report on Form 10-Q for the quarter ended June 30, 2014, as well as the risks, uncertainties and additional information set forth in our SEC reports on Forms 10-K, 10-Q and 8-K and in the other documents incorporated by reference in this prospectus. For a description of these reports and documents, and information about where you can find them, see [Where You Can Find More Information](#) and [Incorporation of Certain Documents By Reference](#). Additional risks not presently known or that we presently consider to be immaterial could subsequently materially and adversely affect our financial condition, results of operations, business and prospects.

- 4 -

Table of Contents**THE COMPANY**

AgenuS Inc. (including its subsidiaries, also referred to as AgenuS, the Company, we, us, and our) is an immuno-oncology company developing a portfolio of checkpoint modulators (CPMs), heat shock protein (HSP)-based vaccines and adjuvants. We are focused on immunotherapeutic products based on our core platform technologies with multiple product candidates advancing through the clinic, including several product candidates that have advanced into late-stage clinical trials through corporate partners. We assess the development, commercialization and/or partnering strategies with respect to each of our internal product candidates periodically based on several factors, including clinical trial results, competitive positioning, and funding requirements and resources.

Our Retrocyte Display® technology platform and CPM antibody programs became part of our portfolio with the acquisition of 4-Antibody AG (4-AB), a European-based biopharmaceutical company, in February 2014. The Retrocyte Display® technology platform is intended to enable, among other things, the rapid generation and optimization of fully-human and humanized monoclonal antibodies against a broad range of target antigens of interest. We currently have six pre-clinical CPM antibody programs, which target GITR, OX40, CTLA-4, PD-1, TIM-3 and LAG-3. Although we envision using Retrocyte Display® to drive the discovery of future CPM antibody candidates, not all candidates will necessarily be derived from the use of this technology. For example, our current antibody candidates targeting GITR were derived independently of Retrocyte Display®. We have selected product candidates targeting GITR (agonists) and CTLA-4 (antagonists) to advance into investigational new drug applications (INDs) enabling development. In addition, we plan to identify development candidates for the other four CPM antibody programs within the next six months, in order to be in a position to file INDs on at least four candidates within the next two years. During the quarter ended June 30, 2014, we entered into a collaboration and license agreement with Merck to discover and optimize fully-human antibodies against two undisclosed cancer targets using the Retrocyte Display®. Under this agreement, Merck will be responsible for the clinical development and commercialization of antibodies generated under the collaboration, and we are eligible to receive approximately \$100 million in potential payments associated with the completion of certain clinical, regulatory and commercial milestones, as well as royalty payments on worldwide product sales. We are exploring other potential partnering opportunities for our Retrocyte Display® technology platform and CPM antibody programs.

Our Prophage Series cancer vaccines are based on our HSP technology platform. Our Prophage Series vaccines are autologous therapies derived from cells extracted from the patient's tumor. As a result, Prophage Series vaccines contain a precise antigenic fingerprint of a patient's particular cancer and are designed to reprogram the body's immune system to target only cells bearing this fingerprint, reducing the risk that powerful anti-cancer agents will target healthy tissue and cause debilitating side effects often associated with chemotherapy and radiation therapy. We believe that in contrast to many other autologous vaccines that are based on cellular preparations, the Prophage Series vaccines are based on a stable protein preparation produced by a less complex manufacturing process. Our Prophage Series vaccines are currently being studied in two different settings of glioblastoma multiforme, or GBM: newly diagnosed and recurrent disease. In July 2014, we announced final results from a single-arm, open-label Phase 2 trial showing that patients with newly-diagnosed glioblastoma who received the Prophage vaccine in addition to the standard of care had a survival benefit over patients who received standard of care alone.

Also within our HSP technology platform is HerpV, a recombinant, synthetic vaccine containing multiple antigens derived from the herpes simplex 2 virus. Combining our HSP technology and our QS-21 Stimulon® adjuvant, HerpV represents a potential new approach to the treatment of genital herpes. In November 2013, we released top line results from a Phase 2, randomized, double blind, multicenter clinical trial of HerpV in HSV-2 positive genital herpes patients, which showed that the trial met its primary endpoint. In June 2014, we announced that the majority of patients showed an immune response to the HSV antigens after a series of vaccinations and a booster dose at six months. More than half of those vaccinated developed a robust anti-HSV cytotoxic T-cell immune response, and in

those patients there was a statistically significant reduction in viral load, which is believed to be relevant in the reduction of transmission and symptoms. After the booster shot,

- 5 -

Table of Contents

HerpV demonstrated a durable reduction in viral shedding approximating 14%, and remains consistent with the reduction in viral shedding observed during the initial treatment period. HerpV evokes immune responses to the mix of HSV2 peptides contained in the vaccine in a substantial majority of patients. We believe that this is the first demonstration of a correlation between immune response and a statistically significant reduction in viral load. We are currently seeking a partner for the further development of our HerpV program. Notwithstanding these data, it is uncertain whether the degree of benefit conferred by HerpV will be sufficient to (i) warrant additional clinical trials funded by us or (ii) attract a development partner.

Our QS-21 Stimulon® vaccine adjuvant is a saponin extracted from the bark of the Quillaja saponaria tree, an evergreen tree native to warm temperate central Chile. QS-21 Stimulon has become a key component in the development of investigational preventive vaccine formulations across a wide variety of infectious diseases and, investigational therapeutic vaccines intended to treat cancer and degenerative disorders. QS-21 Stimulon has been studied in approximately 50,000 patients. Our QS-21 Stimulon is extensively partnered with GlaxoSmithKline (GSK) and JANSSEN Alzheimer Immunotherapy (JANSSEN AI) and includes several vaccine candidates in Phase 2 and Phase 3 clinical trials. In July 2014, GSK submitted to the European Medicines Agency an application for marketing approval of its malaria vaccine candidate incorporating QS-21 Stimulon. If any of our partners' products containing QS-21 Stimulon successfully complete clinical development and receive approval for commercial sale, we are generally entitled to receive milestone payments as well as royalties for 10 years after commercial launch, with some exceptions.

In addition to our internal development efforts, we continue to pursue collaborative, out-licensing and/or partnering opportunities for our portfolio programs and product candidates, as well as explore in-licensing, acquisitions and collaborative arrangements in areas of synergy with our existing programs. Our business activities have included product research and development, intellectual property prosecution, manufacturing, regulatory and clinical affairs, corporate finance and development, business development, and support of our collaborations.

We have financed our operations primarily through the sale of equity and debt securities. We believe that, based on our current plans and activities, our working capital resources at June 30, 2014, plus potential proceeds from our existing license, supply, and collaborative agreements, will be sufficient to satisfy our liquidity requirements through the first half of 2015. We expect to attempt to raise additional funds in advance of depleting our current funds. We may attempt to raise funds by: (1) pursuing collaborative, out-licensing and/or partnering opportunities for our portfolio programs and product candidates with one or more third parties, (2) renegotiating third party agreements, (3) selling assets, (4) securing additional debt financing and/or (5) selling equity securities. Satisfying long-term liquidity needs may require the successful commercialization and/or substantial out-licensing or partnering arrangements for our Retrocyte Display® technology platform, CPM antibody programs, HerpV and the Prophage Series vaccines, and vaccines containing QS-21 Stimulon under development by our licensees. Our long term success will also be dependent on the successful identification, development and commercialization of potential other product candidates, each of which will require additional capital with no certainty of timing or probability of success. If we incur operating losses for longer than we expect and/or we are unable to raise additional capital, we may become insolvent and be unable to continue our operations.

You can find more information about us in our filings with the Securities and Exchange Commission referenced in the sections in this document titled "Incorporation of Certain Documents by Reference" and "Where You Can Find More Information" beginning on pages 2 and 40, respectively.

Table of Contents

USE OF PROCEEDS

This prospectus relates to the securities that may be offered and sold from time to time by us. We expect to use the net proceeds from the sale of the securities from offerings under this prospectus for general corporate purposes unless the applicable prospectus supplement states otherwise. General corporate purposes may include working capital, capital expenditures, repayment and refinancing of debt, research and development expenditures, clinical trial expenditures, acquisitions of additional companies or technologies and investments. We may temporarily invest the net proceeds in investment-grade, interest-bearing securities until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

- 7 -

Table of Contents**RATIO OF EARNINGS TO FIXED CHARGES**

	Six Months Ended		Years Ended December 31,			
	June 30, 2014	2013	2012	2011	2010	2009
Ratio of Earnings to Fixed Charges						
Deficiency of Earnings to Cover						
Fixed Charges	\$ (8,399)	\$ (30,073)	\$ (11,325)	\$ (23,276)	\$ (21,906)	\$ (30,318)
Ratio of Earnings to Combined						
Fixed Charges and Preferred Stock						
Dividends						
Deficiency of Earnings to Cover						
Combined Fixed Charges and						
Preferred Stock Dividends	\$ (8,501)	\$ (33,233)	\$ (12,117)	\$ (24,066)	\$ (22,696)	\$ (31,108)

For purposes of the ratio of earnings to fixed charges and the ration of combined fixed charges and preferred stock dividends to earnings, earnings consist of income before income taxes, interest and the portions of rentals representative of the interest factor. Fixed charges consist of interest expense and the portions of rentals representative of the interest factor.

Table of Contents

DILUTION

If there is a material dilution of the investor's equity interest from the sale of common equity securities offered under this prospectus, we will set forth in any prospectus supplement the following information regarding any such material dilution of the equity interests of purchasers purchasing securities in an offering under this prospectus:

the net tangible book value per share of our equity securities before and after the offering;

the amount of the increase in such net tangible book value per share attributable to the cash payments made by purchasers in the offering; and

the amount of the immediate dilution from the public offering price which will be absorbed by such purchasers.

- 9 -

Table of Contents

DESCRIPTION OF SECURITIES

The descriptions of the securities contained in this prospectus, together with the applicable prospectus supplements, summarize the material terms and provisions of the various types of securities that we may offer. We will describe in the applicable prospectus supplement relating to any securities the particular terms of the securities offered by that prospectus supplement. If we so indicate in the applicable prospectus supplement, the terms of the securities may differ from the terms we have summarized below. We will also include in the prospectus supplement information, where applicable, about material U.S. federal income tax considerations relating to the securities, and the securities exchange, if any, on which the securities will be listed.

We may sell from time to time common stock, preferred stock, debt securities, warrants to purchase any such securities or any combination of the foregoing.

In this prospectus, we refer to the common stock, preferred stock, debt securities and warrants to be sold by us collectively as securities. The total dollar amount of all securities that we may issue under the registration statement of which this prospectus forms a part will not exceed \$150,000,000.

If we issue debt securities at a discount from their original stated principal amount, then we will use the issue price, and not the principal amount, of such debt securities for purposes of calculating the total dollar amount of all securities issued under this prospectus.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

Table of Contents

DESCRIPTION OF CAPITAL STOCK

Agenus is authorized to issue up to 140,000,000 shares of common stock, par value \$0.01 per share, with 62,684,465 shares issued as of September 30, 2014. Agenus is also authorized to issue up to 5,000,000 shares of preferred stock, par value \$0.01 per share, with 31,620 Series A-1 convertible preferred stock issued as of September 30, 2014.

The following description of the Agenus capital stock does not purport to be complete and is qualified in all respects by reference to Agenus' restated certificate of incorporation and bylaws, and the Delaware General Corporation Law (the "DGCL").

- 11 -

Table of Contents

DESCRIPTION OF COMMON STOCK

General

Each share of Agenesis common stock has the same relative rights and is identical in all respects with each other share of common stock.

Voting Rights

Subject to preferences that may apply to shares of preferred stock outstanding at the time, the holders of outstanding shares of common stock are entitled to receive dividends out of assets legally available for payment of dividends, as the board may from time to time determine. Each stockholder is entitled to one vote for each share of common stock held on all matters submitted to a vote of stockholders. Our certificate of incorporation does not provide for cumulative voting for the election of directors, which means that the holders of a majority of the shares voted can elect all of the directors then standing for election. The common stock is not entitled to preemptive rights and is not subject to conversion or redemption. Each outstanding share of common stock offered by this prospectus will, when issued, be fully paid and nonassessable.

Dividends

Holders of common stock are entitled to share ratably in any dividends declared by our board of directors, subject to any preferential dividend rights of any outstanding preferred stock. Dividends consisting of shares of common stock may be paid to holders of shares of common stock. We have never declared or paid cash dividends on our common stock. We do not intend to pay cash dividends in the foreseeable future.

Preemptive Rights

Holders of common stock do not have any preemptive rights with respect to any shares that may be issued by Agenesis in the future. Thus, Agenesis may sell shares of its common stock without first offering them to the then holders of common stock.

Liquidation

In the event of any liquidation or dissolution of Agenesis, whether voluntary or involuntary, the holders of Agenesis common stock would be entitled to receive pro rata, after payment of all debts and liabilities of Agenesis, all assets of Agenesis available for distribution, subject to the rights of the holders of any preferred stock which may be issued with a priority in liquidation or dissolution over the holders of common stock.

Listing

Our common stock is listed on The NASDAQ Capital Market under the symbol AGEN. On October 8, 2014, the last reported sale price for our common stock on The NASDAQ Capital Market was \$2.81 per share. As of October 6, 2014, we had approximately 1,382 stockholders of record.

Anti-Takeover Provisions

Statutory Business Combination Provision

Delaware has adopted a business combination statute (Section 203 of the DGCL) that may also have additional anti-takeover effects to provisions in Agenesis' restated certificate of incorporation and bylaws. Section 203 of the DGCL, which, subject to certain exceptions, prohibits a Delaware corporation from engaging in any business combination with an interested stockholder for a period of three years following the time that such stockholder became an interested stockholder, unless:

the board of directors of the corporation approves either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder, prior to the time the interested stockholder attained that status;

- 12 -

Table of Contents

upon the closing of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding, for purposes of determining the number of shares outstanding, those shares owned by persons who are directors and also officers and by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

at or subsequent to such time, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

With certain exceptions, an interested stockholder is a person or group who or which owns 15% or more of the corporation's outstanding voting stock (including any rights to acquire stock pursuant to an option, warrant, agreement, arrangement or understanding, or upon the exercise of conversion or exchange rights, and stock with respect to which the person has voting rights only), or is an affiliate or associate of the corporation and was the owner of 15% or more of such voting stock at any time within the previous three years.

In general, Section 203 defines a business combination to include:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;

subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; or

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

A Delaware corporation may opt out of this provision with an express provision in its original certificate of incorporation or an express provision in its amended and restated certificate of incorporation or bylaws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. However, Agenus has not opted out of this provision. Section 203 could prohibit or delay mergers or other takeover or change-in-control attempts and, accordingly, may discourage attempts to acquire Agenus.

Size of the Board and Vacancies

Our bylaws provide that the exact number of directors is determined by resolution of the board of directors or by the stockholders at the annual meeting. Our board of directors has the right to fill any vacancies resulting from death,

resignation, disqualification or removal, as well as any newly created directorships arising from an increase in the size of the board.

Amendment of Charter Provisions

The affirmative vote of the holders of at least a majority of the voting power of all then outstanding shares of our voting stock, voting together as a single class, is required to, among other things, amend, alter, change or repeal certain provisions of our restated certificate of incorporation. Our bylaws may only be amended (or new bylaws adopted) by the board of directors or the affirmative vote of the holders of at least a majority of the voting power of all then outstanding shares of our voting stock represented in person or by proxy at the meeting at which the amendment is voted on.

- 13 -

Table of Contents

Undesignated Preferred Stock

We could issue preferred stock that could have other rights, including economic rights senior to our common stock, so that the issuance of the preferred stock could adversely affect the market value of our common stock. The issuance of the preferred stock may also have the effect of delaying, deferring or preventing a change in control of Agenesis without any action by the stockholders. The effects of issuing preferred stock could include one or more of the following:

restricting dividends on the common stock;

diluting the voting power of the common stock;

impairing the liquidation rights of the common stock; or

discouraging, delaying or preventing changes in control or management of Agenesis.

Transfer Agent

The transfer agent and registrar for Agenesis common stock is American Stock Transfer & Trust Company. Its telephone number is (800) 937-5449.

Table of Contents**DESCRIPTION OF PREFERRED STOCK**

We currently have authorized 5,000,000 shares of preferred stock, of which 31,620 shares have been designated as series A-1 convertible preferred stock, 10,000 shares have been designated as series B1 convertible preferred stock, and 5,250 have been designated as series B2 convertible preferred stock. As of the date of this prospectus, all of the series A-1 convertible preferred stock is issued and outstanding in the amount described in the preceding sentence. As of the date of this prospectus, none of the shares of Series B1 convertible preferred stock or Series B2 convertible preferred stock are issued or outstanding. The remaining 4,953,130 authorized shares of preferred stock are undesignated and not issued or outstanding as of the date of this prospectus. As of the date of this prospectus, we do not have any equity securities that would be senior to, or on par with, our authorized preferred stock.

Series A Preferred Stock

On September 24, 2003, we sold 31,620 shares of series A convertible preferred stock, par value \$.01 per share, which we refer to as series A preferred stock. Under the terms and conditions of the Certificate of Designation creating the series A preferred stock, the stock is convertible by the holder at any time into shares of our common stock, is non-voting, carries a 2.5 percent annual dividend yield, has an initial conversion price of \$94.86, and is redeemable by us at its face amount on or after September 24, 2013. In February 2013, we entered into a Securities Exchange Agreement with the holder of our series A preferred stock pursuant to which the holder exchanged all 31,620 of the then outstanding shares of our series A preferred stock for an equivalent number of shares of series A-1 convertible preferred stock (series A-1 preferred stock). The terms of the series A-1 preferred stock are materially identical to the series A preferred stock, except that shares of the series A-1 preferred stock accrue a 0.63% annual dividend, as compared to a 2.5% annual dividend for the series A preferred stock. After giving effect to the transaction, no shares of the series A preferred stock remain outstanding. The liquidation value of the series A-1 preferred stock is equal to \$1,000 per share outstanding plus any accrued and unpaid dividends. The Certificate of Designation does not restrict the repurchase or redemption of shares by us while there is an arrearage in the payment of dividends. The Certificate of Designation does not contemplate a sinking fund. This description of the series A-1 preferred stock is qualified in its entirety by reference to the Certificate of Designation.

Series B Preferred Stock

On September 10, 2007, we issued 10,000 shares of our series B1 convertible preferred stock and 5,250 shares of our series B2 convertible preferred stock (the series B1 convertible preferred stock and the series B2 convertible preferred stock are referred to collectively as the class B convertible preferred stock) to a single institutional investor. In April 2008, all of the series B1 convertible preferred stock was converted into 264,199 shares of our common stock via a cashless conversion. Shares of the series B2 convertible preferred stock permitted the investor to purchase common shares for consideration of up to 35 percent of the total dollar amount previously invested pursuant to an agreement with the investor, including conversions of the series B1 convertible preferred stock, at a purchase price equal to the lesser of \$24.96 per common share or a price calculated based on the then-prevailing price of our common stock. The total number of shares of common stock that were issuable to the holder of the class B convertible preferred stock could not have exceeded 19.9% of our outstanding common stock. In April 2009, we issued 988,202 shares of our common stock upon conversion of 2,145 shares of our series B2 convertible preferred stock via cashless conversions. No dividends were paid on the class B convertible preferred stock and there are no liquidation preferences. In September 2014, all issued and outstanding shares of Series B2 convertible preferred stock were cancelled and extinguished in accordance with the Certificate of Designation. This description of the class B convertible preferred stock is qualified in its entirety by reference to the Certificate of Designation.

Undesignated Preferred Stock

This section describes the general terms and provisions of the preferred stock that we may offer by this prospectus. The prospectus supplement will describe the specific terms of the series of the preferred stock offered

- 15 -

Table of Contents

through that prospectus supplement. Those terms may differ from the terms discussed below. Any series of preferred stock we will issue will be governed by our restated certificate of incorporation, as amended, including the certificate of designations relating to such series of preferred stock, and our bylaws, as amended. In this section entitled

Description of Preferred Stock, references to Agenus, we, our and us refer only to Agenus Inc. and not to its consolidated subsidiaries.

We will fix the rights, preferences, privileges and restrictions of the preferred stock of each series in the certificate of designations relating to that series. We will incorporate by reference as an exhibit to the registration statement that includes this prospectus the form of any certificate of designations which describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. This description will include the following, to the extent applicable:

the title and stated value;

the number of shares we are offering;

the liquidation preference per share;

the purchase price;

the dividend rate, period and payment date, and method of calculation for dividends, if any;

whether any dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

the provisions for a sinking fund, if any;

the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock and, if applicable, the conversion price, or how it will be calculated, and the conversion period;

whether the preferred stock will be exchangeable into debt securities and, if applicable, the exchange price, or how it will be calculated, and the exchange period;

voting rights, if any, of the preferred stock;

preemptive rights, if any;

restrictions on transfer, sale or other assignment, if any;

whether interests in the preferred stock will be represented by depositary shares;

a discussion of any material or special United States federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

When we issue shares of preferred stock under this prospectus, the shares, when issued in accordance with the terms of the applicable agreement, will be validly issued, fully paid and non-assessable and will not have, or be subject to, any preemptive or similar rights.

Section 242 of DGCL provides that the holders of each class or series of stock will have the right to vote separately as a class on certain amendments to our restated certificate of incorporation that would affect the class or series of preferred stock, as applicable. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Table of Contents

DESCRIPTION OF WARRANTS

We may issue warrants or other rights. We may issue these securities in such amounts or in as many distinct series as we wish. This section summarizes the terms of these securities that apply generally. We will describe the financial and other specific terms of any such series of securities in the prospectus supplement accompanying this prospectus. Those terms may vary from the terms described here.

When we refer to a series of securities in this section, we mean all securities issued as part of the same series under any applicable indenture, agreement or other instrument. When we refer to the prospectus supplement, we mean the applicable prospectus supplement describing the specific terms of the security you purchase. The terms used in the prospectus supplement will have the meanings described in this prospectus, unless otherwise specified.

In this section entitled Description of Warrants, references to Agenus, we, our and us refer only to Agenus Inc. and its consolidated subsidiaries. Also, in this section, references to holders mean those who own warrants or other rights registered in their own names, on the books that we or any applicable trustee or warrant or rights agent maintain for this purpose, and not those who own beneficial interests in warrants registered in street name or in warrants issued in book-entry form through one or more depositaries. Owners of beneficial interests in warrants should also read the section entitled Legal Ownership and Book-Entry Issuance.

Warrants

The following description of warrants does not purport to be complete and is qualified in its entirety by reference to the description of a particular series of warrants contained in an applicable prospectus supplement. For information relating to common stock and preferred stock, see Description of Common Stock and Description of Preferred Stock, respectively.

We may offer by means of this prospectus warrants for the purchase of our preferred stock or common stock. We may issue warrants separately or together with any other securities offered by means of this prospectus, and the warrants may be attached to or separate from such securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a warrant agent specified therein. The warrant agent will act solely as our agent in connection with the warrants of such series and will not assume any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants.

Agreements

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any warrants we issue pursuant to this prospectus. Each series of warrants may be evidenced by certificates and may be issued under a separate indenture, agreement or other instrument to be entered into between us and a bank that we select as agent with respect to such series. The agent, if any, will have its principal office in the U.S. and have a combined capital and surplus of at least \$50,000,000. Warrants in book-entry form will be represented by a global security registered in the name of a depositary, which will be the holder of all the securities represented by the global security. Those who own beneficial interests in a global security will do so through participants in the depositary's system, and the rights of these indirect owners will be governed solely by the applicable procedures of the depositary and its participants. We describe book-entry securities under Legal Ownership and Book-Entry Issuance.

General Terms of Warrants

The prospectus supplement relating to a series of warrants will identify the name and address of the warrant agent, if any. The prospectus supplement will describe the following terms, where applicable, of the warrants in respect of which this prospectus is being delivered:

the title and issuer of the warrants;

the aggregate number of warrants;

- 17 -

Table of Contents

the price or prices at which the warrants will be issued;

the currencies in which the price or prices of the warrants may be payable;

the designation, amount and terms of the securities purchasable upon exercise of the warrants;

the designation and terms of the other securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of security;

if applicable, the date on and after which the warrants and any related securities will be separately transferable;

any securities exchange or quotation system on which the warrants or any securities deliverable upon exercise of such securities may be listed;

the price or prices at which and currency or currencies in which the securities purchasable upon exercise of the warrants may be purchased;

the date on which the right to exercise the warrants shall commence and the date on which such right shall expire;

the minimum or maximum amount of warrants that may be exercised at any one time;

whether the warrants will be issued in fully registered for or bearer form, in global or non-global form or in any combination of these forms;

information with respect to book-entry procedures, if any;

a discussion of certain U.S. federal income tax considerations; and

any other material terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Exercise of Warrants

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any warrants we issue pursuant to this prospectus. If any warrant is exercisable for other securities or other property, the

following provisions will apply. Each such warrant may be exercised at any time up to any expiration date and time mentioned in the prospectus supplement relating to those warrants. After the close of business on any applicable expiration date, unexercised warrants will become void.

Warrants may be exercised by delivery of the certificate representing the securities to be exercised, or in the case of global securities, as described below under Legal Ownership and Book-Entry Issuance, by delivery of an exercise notice for those warrants, together with certain information, and payment to any agent in immediately available funds, as provided in the prospectus supplement, of the required purchase amount, if any. Upon receipt of payment and the certificate or exercise notice properly executed at the office indicated in the prospectus supplement, we will, in the time period the relevant agreement provides, issue and deliver the securities or other property purchasable upon such exercise. If fewer than all of the warrants represented by such certificates are exercised, a new certificate will be issued for the remaining amount of warrants.

If mentioned in the prospectus supplement, securities may be surrendered as all or part of the exercise price for warrants.

Antidilution Provisions

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any warrants we issue pursuant to this prospectus. In the case of warrants to purchase common stock, the exercise price payable and the number of shares of common stock purchasable upon warrant exercise may be adjusted in certain events, including:

the issuance of a stock dividend to common shareholders or a combination, subdivision or reclassification of common stock;

Table of Contents

the issuance of rights, warrants or options to all common and preferred shareholders entitling them to purchase common stock for an aggregate consideration per share less than the current market price per share of common stock;

any distribution to our common shareholders of evidences of our indebtedness of assets, excluding cash dividends or distributions referred to above; and

any other events mentioned in the prospectus supplement.

The prospectus supplement will describe which, if any, of these provisions shall apply to a particular series of warrants. Unless otherwise specified in the applicable prospectus supplement, no adjustment in the number of shares purchasable upon warrant exercise will be required until cumulative adjustments require an adjustment of at least 1% of such number and no fractional shares will be issued upon warrant exercise, but we will pay the cash value of any fractional shares otherwise issuable.

Modification

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any warrants we issue pursuant to this prospectus. We and any agent for any series of warrants may amend any warrant or rights agreement and the terms of the related warrants by executing a supplemental agreement, without any such warrantholders' consent, for the purpose of:

curing any ambiguity, any defective or inconsistent provision contained in the agreement, or making any other corrections to the agreement that are not inconsistent with the provisions of the warrant certificates;

evidencing the succession of another corporation to us and its assumption of our covenants contained in the agreement and the securities;

appointing a successor depository, if the securities are issued in the form of global securities;

evidencing a successor agent's acceptance of appointment with respect to any securities;

adding to our covenants for the benefit of securityholders or surrendering any right or power we have under the agreement;

issuing warrants in definitive form, if such securities are initially issued in the form of global securities; or

amending the agreement and the warrants as we deem necessary or desirable and that will not adversely affect the interests of the applicable warrantholders in any material respect.

We and any agent for any series of warrants may also amend any agreement and the related warrants by a supplemental agreement with the consent of the holders of a majority of the warrants of any series affected by such amendment, for the purpose of adding, modifying or eliminating any of the agreement's provisions or of modifying the rights of the holders of warrants. However, no such amendment that:

reduces the number or amount of securities receivable upon any exercise of any such security;

shortens the time period during which any such security may be exercised;

otherwise adversely affects the exercise rights of warrantholders in any material respect; or

reduces the number of securities the consent of holders of which is required for amending the agreement or the related warrants;

may be made without the consent of each holder affected by that amendment.

Table of Contents

Consolidation, Merger and Sale of Assets

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any warrants we issue pursuant to this prospectus. Any agreement with respect to warrants will provide that we are generally permitted to merge or consolidate with another corporation or other entity. Any such agreement will also provide that we are permitted to sell our assets substantially as an entirety to another corporation or other entity or to have another entity sell its assets substantially as an entirety to us. With regard to any series of warrants, however, we may not take any of these actions unless all of the following conditions are met:

if we are not the successor entity, the person formed by the consolidation or into or with which we merge or the person to which our properties and assets are conveyed, transferred or leased must be an entity organized and existing under the laws of the United States, any state or the District of Columbia and must expressly assume the performance of our covenants under any relevant indenture, agreement or other instrument; and

we or that successor corporation must not immediately be in default under that agreement.

Enforcement by Holders of Warrants

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any warrants we issue pursuant to this prospectus. Any agent for any series of warrants will act solely as our agent under the relevant agreement and will not assume any obligation or relationship of agency or trust for any securityholder. A single bank or trust company may act as agent for more than one issue of securities. Any such agent will have no duty or responsibility in case we default in performing our obligations under the relevant agreement or warrant, including any duty or responsibility to initiate any legal proceedings or to make any demand upon us. Any securityholder may, without the agent's consent or consent of any other securityholder, enforce by appropriate legal action its right to exercise any warrant exercisable for any property.

Replacement of Certificates

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any warrants we issue pursuant to this prospectus. We will replace any destroyed, lost, stolen or mutilated warrant or rights certificate upon delivery to us and any applicable agent of satisfactory evidence of the ownership of that certificate and of its destruction, loss, theft or mutilation, and (in the case of mutilation) surrender of that certificate to us or any applicable agent, unless we have, or the agent has, received notice that the certificate has been acquired by a bona fide purchaser. That securityholder will also be required to provide indemnity satisfactory to us and the relevant agent before a replacement certificate will be issued.

Title

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any warrants we issue pursuant to this prospectus. We, any agents for any series of warrants and any of their agents may treat the registered holder of any certificate as the absolute owner of the securities evidenced by that certificate for any purpose and as the person entitled to exercise the rights attaching to the warrants so requested, despite any notice to the contrary. See Legal Ownership and Book-Entry Issuance.

Table of Contents

DESCRIPTION OF DEBT SECURITIES

We will issue the debt securities offered by this prospectus and any accompanying prospectus supplement under an indenture to be entered into between Agenesis and the trustee identified in the applicable prospectus supplement. The terms of the debt securities will include those stated in the indenture and those made part of the indenture by reference to the Trust Indenture Act of 1939, as in effect on the date of the indenture. We have filed a copy of the form of indenture as an exhibit to the registration statement in which this prospectus is included. The indenture will be subject to and governed by the terms of the Trust Indenture Act of 1939.

We may offer under this prospectus up to an aggregate principal amount of \$150,000,000 in debt securities; or if debt securities are issued at a discount, or in a foreign currency, foreign currency units or composite currency, the principal amount as may be sold for an initial public offering price of up to \$150,000,000. Unless otherwise specified in the applicable prospectus supplement, the debt securities will represent direct, unsecured obligations of Agenesis and will rank equally with all of our other unsecured indebtedness.

The following statements relating to the debt securities and the indenture are summaries, qualified in their entirety to the detailed provisions of the indenture.

General

We may issue the debt securities in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will describe the particular terms of each series of debt securities in a prospectus supplement relating to that series, which we will file with the SEC.

The prospectus supplement will set forth, to the extent required, the following terms of the debt securities in respect of which the prospectus supplement is delivered:

the title of the series;

the aggregate principal amount;

the issue price or prices, expressed as a percentage of the aggregate principal amount of the debt securities;

any limit on the aggregate principal amount;

the date or dates on which principal is payable;

the interest rate or rates (which may be fixed or variable) or, if applicable, the method used to determine such rate or rates;

the date or dates from which interest, if any, will be payable and any regular record date for the interest payable;

the place or places where principal and, if applicable, premium and interest, is payable;

the terms and conditions upon which we may, or the holders may require us to, redeem or repurchase the debt securities;

the denominations in which such debt securities may be issuable, if other than denominations of \$1,000, or any integral multiple of that number;

whether the debt securities are to be issuable in the form of certificated debt securities (as described below) or global debt securities (as described below);

the portion of principal amount that will be payable upon declaration of acceleration of the maturity date if other than the principal amount of the debt securities;

Table of Contents

the currency of denomination;

the designation of the currency, currencies or currency units in which payment of principal and, if applicable, premium and interest, will be made;

if payments of principal and, if applicable, premium or interest, on the debt securities are to be made in one or more currencies or currency units other than the currency of denomination, the manner in which the exchange rate with respect to such payments will be determined;

if amounts of principal and, if applicable, premium and interest may be determined by reference to an index based on a currency or currencies, or by reference to a commodity, commodity index, stock exchange index, or financial index, then the manner in which such amounts will be determined;

the provisions, if any, relating to any collateral provided for such debt securities;

any addition to or change in the covenants and/or the acceleration provisions described in this prospectus or in the indenture;

any events of default, if not otherwise described below under Events of Default ;

the terms and conditions, if any, for conversion into or exchange for shares of common stock or preferred stock;

any depositaries, interest rate calculation agents, exchange rate calculation agents, or other agents; and

the terms and conditions, if any, upon which the debt securities shall be subordinated in right of payment to other indebtedness of Agenus.

We may issue discount debt securities that provide for an amount less than the stated principal amount to be due and payable upon acceleration of the maturity of such debt securities in accordance with the terms of the indenture. We may also issue debt securities in bearer form, with or without coupons. If we issue discount debt securities or debt securities in bearer form, we will describe material U.S. federal income tax considerations and other material special considerations which apply to these debt securities in the applicable prospectus supplement.

We may issue debt securities denominated in or payable in a foreign currency or currencies or a foreign currency unit or units. If we do, we will describe the restrictions, elections, and general tax considerations relating to the debt securities and the foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Exchange and/or Conversion Rights

We may issue debt securities which can be exchanged for or converted into shares of common stock or preferred stock. If we do, we will describe the terms of exchange or conversion in the prospectus supplement relating to these debt securities.

Transfer and Exchange

We may issue debt securities that will be represented by either:

book-entry securities, which means that there will be one or more global securities registered in the name of a depositary or a nominee of a depositary; or

certificated securities, which means that they will be represented by a certificate issued in definitive registered form.

We will specify in the prospectus supplement applicable to a particular offering whether the debt securities offered will be book-entry or certificated securities.

- 22 -

Table of Contents

Certificated Debt Securities

Those who hold certificated debt securities may transfer or exchange such debt securities at the trustee's office or at the paying agent's office or agency in accordance with the terms of the indenture. There will be no service charge for any transfer or exchange of certificated debt securities but there may be a requirement to pay an amount sufficient to cover any tax or other governmental charge payable in connection with such transfer or exchange.

Those who hold certificated debt securities may effect the transfer of certificated debt securities and of the right to receive the principal of, premium, and/or interest, if any, on the certificated debt securities only by surrendering the certificate representing the certificated debt securities and having us or the trustee issue a new certificate to the new holder.

Global Securities

If we decide to issue debt securities in the form of one or more global securities, then we will register the global securities in the name of the depositary for the global securities or the nominee of the depositary, and the global securities will be delivered by the trustee to the depositary for credit to the accounts of the holders of beneficial interests in the debt securities.

The prospectus supplement will describe the specific terms of the depositary arrangement for debt securities of a series that are issued in global form. None of the Company, the trustee, any payment agent, or the security registrar will have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial ownership interests in a global debt security or for maintaining, supervising, or reviewing any records relating to these beneficial ownership interests.

No Protection in the Event of Change of Control

The indenture does not have any covenants or other provisions providing for a put or increased interest or otherwise that would afford holders of debt securities additional protection in the event of a recapitalization transaction, a change of control of Agenus, or a highly leveraged transaction. If we offer any covenants or provisions of this type with respect to any debt securities covered by this prospectus, we will describe them in the applicable prospectus supplement.

Covenants

Unless otherwise indicated in this prospectus or a prospectus supplement, the debt securities will not have the benefit of any covenants that limit or restrict our business or operations, the pledging of our assets, or the incurrence by us of indebtedness. We will describe in the applicable prospectus supplement any material covenants in respect of a series of debt securities.

Consolidation, Merger, and Sale of Assets

We have agreed in the indenture that we will not consolidate with or merge into any other person, or convey, transfer, sell, or lease our properties and assets substantially as an entirety to any person, unless:

the person formed by the consolidation or into or with which we are merged or the person to which our properties and assets are conveyed, transferred, sold, or leased, is a corporation organized and existing under the laws of the U.S., any state or the District of Columbia, or a corporation or comparable legal entity organized under the laws of a foreign jurisdiction and, if we are not the surviving person, the surviving person has expressly assumed all of our obligations, including the payment of the principal of, and premium, if any, and interest on the debt securities and the performance of the other covenants under the indenture; and

- 23 -

Table of Contents

immediately after giving effect to the transaction, no event of default, and no event which, after notice or lapse of time or both, would become an event of default, has occurred and is continuing under the indenture.

Events of Default

Unless otherwise specified in the applicable prospectus supplement, the following events will be events of default under the indenture with respect to debt securities of any series:

we fail to pay any principal or premium, if any, when it becomes due;

we fail to pay any interest within 30 days after it becomes due;

we fail to comply with any other covenant in the debt securities or the indenture for 60 days after written notice specifying the failure from the trustee or the holders of not less than 25% in aggregate principal amount of the outstanding debt securities of that series; and

certain events involving bankruptcy, insolvency, or reorganization of Agenus or any of our significant subsidiaries.

The trustee may withhold notice to the holders of the debt securities of any series of any default, except in payment of principal of, or premium, if any, or interest on the debt securities of a series, if the trustee considers it to be in the best interest of the holders of the debt securities of that series to do so.

If an event of default (other than an event of default resulting from certain events of bankruptcy, insolvency, or reorganization) occurs, and is continuing, then the trustee or the holders of not less than 25% in aggregate principal amount of the outstanding debt securities of any series may accelerate the maturity of the debt securities. If this happens, the entire principal amount, plus the premium, if any, of all the outstanding debt securities of the affected series plus accrued interest to the date of acceleration will be immediately due and payable. At any time after the acceleration, but before a judgment or decree based on such acceleration is obtained by the trustee, the holders of a majority in aggregate principal amount of outstanding debt securities of such series may rescind and annul such acceleration if:

all events of default (other than nonpayment of accelerated principal, premium, or interest) have been cured or waived;

all lawful interest on overdue interest and overdue principal has been paid; and

the rescission would not conflict with any judgment or decree.

In addition, if the acceleration occurs at any time when Agenus has outstanding indebtedness which is senior to the debt securities, the payment of the principal amount of outstanding debt securities may be subordinated in right of payment to the prior payment of any amounts due under the senior indebtedness, in which case the holders of debt

securities will be entitled to payment under the terms prescribed in the instruments evidencing the senior indebtedness and the indenture.

If an event of default resulting from certain events of bankruptcy, insolvency, or reorganization occurs, the principal, premium, and interest amount with respect to all of the debt securities of any series will be due and payable immediately without any declaration or other act on the part of the trustee or the holders of the debt securities of that series.

The holders of a majority in principal amount of the outstanding debt securities of a series will have the right to waive any existing default or compliance with any provision of the indenture or the debt securities of that series and to direct the time, method, and place of conducting any proceeding for any remedy available to the trustee, subject to certain limitations specified in the indenture.

- 24 -

Table of Contents

No holder of any debt security of a series will have any right to institute any proceeding with respect to the indenture or for any remedy under the indenture, unless:

the holder gives to the trustee written notice of a continuing event of default;

the holders of at least 25% in aggregate principal amount of the outstanding debt securities of the affected series make a written request and offer reasonable indemnity to the trustee to institute a proceeding as trustee;

the trustee fails to institute a proceeding within 60 days after such request; and

the holders of a majority in aggregate principal amount of the outstanding debt securities of the affected series do not give the trustee a direction inconsistent with such request during such 60-day period.

These limitations do not, however, apply to a suit instituted for payment on debt securities of any series on or after the due dates expressed in the debt securities.

Modification and Waiver

From time to time, we and the trustee may, without the consent of holders of the debt securities of one or more series, amend the indenture or the debt securities of one or more series, or supplement the indenture, for certain specified purposes, including:

to provide that the surviving entity following a change of control of Agenus permitted under the indenture will assume all of our obligations under the indenture and debt securities;

to provide for certificated debt securities in addition to uncertificated debt securities;

to comply with any requirements of the SEC under the Trust Indenture Act of 1939;

to cure any ambiguity, defect, or inconsistency, or make any other change that does not materially and adversely affect the rights of any holder; and

to appoint a successor trustee under the indenture with respect to one or more series.

From time to time, we and the trustee may, with the consent of holders of at least a majority in principal amount of the outstanding debt securities, amend or supplement the indenture or the debt securities, or waive compliance in a particular instance by us with any provision of the indenture or the debt securities. We may not, however, without the consent of each holder affected by such action, modify or supplement the indenture or the debt securities, or waive

compliance with any provision of the indenture or the debt securities in order to:

reduce the amount of debt securities whose holders must consent to an amendment, supplement, or waiver to the indenture or such debt security;

reduce the rate of or change the time for payment of interest;

reduce the principal of or change the stated maturity of the debt securities;

make any debt security payable in money other than that stated in the debt security;

change the amount or time of any payment required, or reduce the premium payable upon any redemption, or change the time before which no such redemption may be made;

waive a default in the payment of the principal of, premium, if any, or interest on the debt securities or a redemption payment; or

take any other action otherwise prohibited by the indenture to be taken without the consent of each holder affected by the action.

- 25 -

Table of Contents

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

The indenture permits us, at any time, to elect to discharge our obligations with respect to one or more series of debt securities by following certain procedures described in the indenture. These procedures will allow us either:

to defease and be discharged from any and all of our obligations with respect to any debt securities except for the following obligations (which discharge is referred to as "legal defeasance"):

- (1) to register the transfer or exchange of such debt securities;
- (2) to replace temporary or mutilated, destroyed, lost, or stolen debt securities;
- (3) to compensate and indemnify the trustee; or
- (4) to maintain an office or agency in respect of the debt securities and to hold monies for payment in trust; or

to be released from our obligations with respect to the debt securities under certain covenants contained in the indenture, as well as any additional covenants which may be contained in the applicable supplemental indenture (which release is referred to as "covenant defeasance").

In order to exercise either defeasance option, we must deposit with the trustee or other qualifying trustee, in trust for that purpose:

money;

U.S. Government Obligations (as described below) or Foreign Government Obligations (as described below) which through the scheduled payment of principal and interest in accordance with their terms will provide money; or

a combination of money and/or U.S. Government Obligations and/or Foreign Government Obligations sufficient in the written opinion of a nationally-recognized firm of independent accountants to provide money;

which in each case specified above, provides a sufficient amount to pay the principal of, premium, if any, and interest, if any, on the debt securities of the series, on the scheduled due dates or on a selected date of redemption in accordance with the terms of the indenture.

In addition, defeasance may be effected only if, among other things:

in the case of either legal or covenant defeasance, we deliver to the trustee an opinion of counsel, as specified in the indenture, stating that as a result of the defeasance neither the trust nor the trustee will be

required to register as an investment company under the Investment Company Act of 1940;

in the case of legal defeasance, we deliver to the trustee an opinion of counsel stating that we have received from, or there has been published by, the Internal Revenue Service a ruling to the effect that, or there has been a change in any applicable federal income tax law with the effect that (and the opinion shall confirm that), the holders of outstanding debt securities will not recognize income, gain, or loss for U.S. federal income tax purposes solely as a result of such legal defeasance and will be subject to U.S. federal income tax on the same amounts, in the same manner, including as a result of prepayment, and at the same times as would have been the case if legal defeasance had not occurred;

in the case of covenant defeasance, we deliver to the trustee an opinion of counsel to the effect that the holders of the outstanding debt securities will not recognize income, gain, or loss for U.S. federal income tax purposes as a result of covenant defeasance and will be subject to U.S. federal income tax on the same amounts, in the same manner, and at the same times as would have been the case if covenant defeasance had not occurred; and

certain other conditions described in the indenture are satisfied.

Table of Contents

If we fail to comply with our remaining obligations under the indenture and applicable supplemental indenture after a covenant defeasance of the indenture and applicable supplemental indenture, and the debt securities are declared due and payable because of the occurrence of any undefeased event of default, the amount of money and/or U.S. Government Obligations and/or Foreign Government Obligations on deposit with the trustee could be insufficient to pay amounts due under the debt securities of the affected series at the time of acceleration. We will, however, remain liable in respect of these payments.

The term "U.S. Government Obligations" as used in the above discussion means securities which are direct obligations of or non-callable obligations guaranteed by the United States of America for the payment of which obligation or guarantee the full faith and credit of the United States of America is pledged.

The term "Foreign Government Obligations" as used in the above discussion means, with respect to debt securities of any series that are denominated in a currency other than U.S. dollars (1) direct obligations of the government that issued or caused to be issued such currency for the payment of which obligations its full faith and credit is pledged or (2) obligations of a person controlled or supervised by or acting as an agent or instrumentality of such government the timely payment of which is unconditionally guaranteed as a full faith and credit obligation by that government, which in either case under clauses (1) or (2), are not callable or redeemable at the option of the issuer.

Regarding the Trustee

We will identify the trustee with respect to any series of debt securities in the prospectus supplement relating to the applicable debt securities. You should note that if the trustee becomes a creditor of Agenus, the indenture and the Trust Indenture Act of 1939 limit the rights of the trustee to obtain payment of claims in certain cases, or to realize on certain property received in respect of any such claim, as security or otherwise. The trustee and its affiliates may engage in, and will be permitted to continue to engage in, other transactions with us and our affiliates. If, however, the trustee acquires any "conflicting interest" within the meaning of the Trust Indenture Act of 1939, it must eliminate such conflict or resign.

The holders of a majority in principal amount of the then outstanding debt securities of any series may direct the time, method, and place of conducting any proceeding for exercising any remedy available to the trustee. If an event of default occurs and is continuing, the trustee, in the exercise of its rights and powers, must use the degree of care and skill of a prudent person in the conduct of his or her own affairs. Subject to that provision, the trustee will be under no obligation to exercise any of its rights or powers under the indenture at the request of any of the holders of the debt securities, unless they have offered to the trustee reasonable indemnity or security.

Table of Contents

DESCRIPTION OF UNITS

This section outlines some of the provisions of the units and the unit agreements that we may enter into. This information may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units will be described in the applicable prospectus supplement. If so described in a particular supplement, the specific terms of any series of units may differ from the general description of terms presented below.

In this section entitled Description of Units, references to Agenus, we, our and us refer only to Agenus Inc. and its consolidated subsidiaries. Also, in this section, references to holders mean those who own units registered in their own names, on the books that we or our agent maintain for this purpose, and not those who own beneficial interests in units registered in street name or in units issued in book-entry form through one or more depositaries. Owners of beneficial interests in the units should read the section below entitled Legal Ownership and Book-Entry Issuance.

We may issue units comprised of one or more debt securities, shares of common stock, shares of preferred stock, and warrants in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

The applicable prospectus supplement may describe:

the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;

any provisions of the governing unit agreement that differ from those described below; and

any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those described under Description of Common Stock, Description of Preferred Stock, Description of Warrants and Description of Debt Securities will apply to the securities included in each unit, to the extent relevant.

Issuance in Series

We may issue units in such amounts and in as many distinct series as we wish. This section summarizes terms of the units that apply generally to all series. Most of the financial and other specific terms of your series will be described in the applicable prospectus supplement.

Unit Agreements

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any units we issue pursuant to this prospectus. We will issue the units under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. We may add, replace or terminate unit agents from

time to time. We will identify the unit agreement under which each series of units will be issued and the unit agent under that agreement in the applicable prospectus supplement.

The following provisions will generally apply to all unit agreements unless otherwise stated in the applicable prospectus supplement.

- 28 -

Table of Contents

Enforcement of Rights

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any units we issue pursuant to this prospectus. The unit agent under a unit agreement will act solely as our agent in connection with the units issued under that agreement. The unit agent will not assume any obligation or relationship of agency or trust for or with any holders of those units or of the securities comprising those units. The unit agent will not be obligated to take any action on behalf of those holders to enforce or protect their rights under the units or the included securities.

Except as indicated in the next paragraph, a holder of a unit may, without the consent of the unit agent or any other holder, enforce its rights as holder under any security included in the unit, in accordance with the terms of that security and the indenture, warrant agreement, rights agreement or other instrument under which that security is issued. Those terms are described elsewhere in this prospectus under the sections relating to debt securities, preferred stock, common stock or warrants, as relevant.

Notwithstanding the foregoing, a unit agreement may limit or otherwise affect the ability of a holder of units issued under that agreement to enforce its rights, including any right to bring a legal action, with respect to those units or any securities, other than debt securities, that are included in those units. Limitations of this kind will be described in the applicable prospectus supplement.

Modification without Consent of Holders

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any units we issue pursuant to this prospectus. We and the applicable unit agent may amend any unit or unit agreement without the consent of any holder:

to cure any ambiguity;

to correct or supplement any defective or inconsistent provision; or

to make any other change that we believe is necessary or desirable and will not adversely affect the interests of the affected holders in any material respect.

We do not need any approval to make changes that affect only units to be issued after the changes take effect. We may also make changes that do not adversely affect a particular unit in any material respect, even if they adversely affect other units in a material respect. In those cases, we do not need to obtain the approval of the holder of the unaffected unit; we need only obtain any required approvals from the holders of the affected units.

Modification with Consent of Holders

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any units we issue pursuant to this prospectus. We may not amend any particular unit or a unit agreement with respect to any particular unit unless we obtain the consent of the holder of that unit, if the amendment would:

impair any right of the holder to exercise or enforce any right under a security included in the unit if the terms of that security require the consent of the holder to any changes that would impair the exercise or enforcement of that right; or

reduce the percentage of outstanding units or any series or class the consent of whose holders is required to amend that series or class, or the applicable unit agreement with respect to that series or class, as described below.

- 29 -

Table of Contents

Any other change to a particular unit agreement and the units issued under that agreement would require the following approval:

if the change affects only the units of a particular series issued under that agreement, the change must be approved by the holders of a majority of the outstanding units of that series; or

if the change affects the units of more than one series issued under that agreement, it must be approved by the holders of a majority of all outstanding units of all series affected by the change, with the units of all the affected series voting together as one class for this purpose.

These provisions regarding changes with majority approval also apply to changes affecting any securities issued under a unit agreement, as the governing document.

In each case, the required approval must be given by written consent.

Unit Agreements Will Not Be Qualified Under Trust Indenture Act

No unit agreement will be qualified as an indenture, and no unit agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of units issued under unit agreements will not have the protections of the Trust Indenture Act with respect to their units.

Mergers and Similar Transactions Permitted; No Restrictive Covenants or Events of Default

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any units we issue pursuant to this prospectus. The unit agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another corporation or other entity or to engage in any other transactions. If at any time we merge or consolidate with, or sell our assets substantially as an entirety to, another corporation or other entity, the successor entity will succeed to and assume our obligations under the unit agreements. We will then be relieved of any further obligation under these agreements.

The unit agreements will not include any restrictions on our ability to put liens on our assets, including our interests in our subsidiaries, nor will they restrict our ability to sell our assets. The unit agreements also will not provide for any events of default or remedies upon the occurrence of any events of default.

Governing Law

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any units we issue pursuant to this prospectus. The unit agreements and the units will be governed by New York law.

Form, Exchange and Transfer

Unless otherwise provided in the applicable prospectus supplement, the following provisions will apply to any units we issue pursuant to this prospectus. We will issue each unit in global that is, book-entry form only. Units in book-entry form will be represented by a global security registered in the name of a depository, which will be the holder of all the units represented by the global security. Those who own beneficial interests in a unit will do so through participants in the depository's system, and the rights of these indirect owners will be governed solely by the

applicable procedures of the depositary and its participants. We describe book-entry securities below under Legal Ownership and Book-Entry Issuance.

In addition, we will issue each unit in registered form, unless we say otherwise in the applicable prospectus supplement. Bearer securities would be subject to special provisions, as we describe below under Securities Issued in Bearer Form.

- 30 -

Table of Contents

Each unit and all securities comprising the unit will be issued in the same form.

If we issue any units in registered, non-global form, the following will apply to them.

The units will be issued in the denominations stated in the applicable prospectus supplement. Holders may exchange their units for units of smaller denominations or combined into fewer units of larger denominations, as long as the total amount is not changed.

Holders may exchange or transfer their units at the office of the unit agent. Holders may also replace lost, stolen, destroyed or mutilated units at that office. We may appoint another entity to perform these functions or perform them ourselves.

Holders will not be required to pay a service charge to transfer or exchange their units, but they may be required to pay for any tax or other governmental charge associated with the transfer or exchange. The transfer or exchange, and any replacement, will be made only if our transfer agent is satisfied with the holder's proof of legal ownership. The transfer agent may also require an indemnity before replacing any units.

If we have the right to redeem, accelerate or settle any units before their maturity, and we exercise our right as to less than all those units or other securities, we may block the exchange or transfer of those units during the period beginning 15 days before the day we mail the notice of exercise and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers of or exchange any unit selected for early settlement, except that we will continue to permit transfers and exchanges of the unsettled portion of any unit being partially settled. We may also block the transfer or exchange of any unit in this manner if the unit includes securities that are or may be selected for early settlement.

Only the depositary will be entitled to transfer or exchange a unit in global form, since it will be the sole holder of the unit.

Payments and Notices

In making payments and giving notices with respect to our units, we will follow the procedures we plan to use with respect to our debt securities, where applicable.

Table of Contents

LEGAL OWNERSHIP AND BOOK-ENTRY ISSUANCE

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable depositary or warrant agent maintain for this purpose as the **holders** of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as **indirect holders** of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

Except as described below, we will issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Global securities will be registered in the name of the depositary or its participants. Consequently, for global securities, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not legal holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities that are not issued in global form. In these cases, investors may choose to hold their securities in their own names or in **street name**. Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we or any applicable depositary will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we or any such depositary will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not legal holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable depositary or warrant agent or other third party employed by us or any of the foregoing, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

- 32 -

Table of Contents

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an instrument defining the rights of security holders, to relieve us of the consequences of a breach or of our or its obligation to comply with a particular provision of such an instrument or for other purposes. In such an event, we would seek approval only from the legal holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the legal holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

how it handles securities payments and notices;

whether it imposes fees or charges;

how it would handle a request for the holders' consent, if ever required;

whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;

how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and

if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless specified otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York ("DTC"), will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under "Special Situations When a Global Security Will Be Terminated." As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by

means of an account with a broker, bank or other financial institution that in turn has an account with the depository or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Table of Contents

Special Considerations for Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a legal holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

An investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below.

An investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above.

An investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form.

An investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective.

The depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security. We and any applicable agent have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security. We and any applicable agent also will not supervise the depositary in any way.

The depositary may, and we understand that DTC will, require that those who purchase and sell interests in the global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well.

Financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in the global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When A Global Security Will Be Terminated

In a few special situations described below, the global security will terminate, and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

The global security will terminate when the following special situations occur:

if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;

if we notify any applicable depositary or warrant agent that we wish to terminate that global security; or

if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

- 34 -

Table of Contents

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depositary, and not us or any applicable agent, is responsible for deciding the names of the institutions that will be the initial direct holders.

- 35 -

Table of Contents

PLAN OF DISTRIBUTION

We may sell the securities covered by this prospectus directly to purchasers or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions from us. These discounts, concessions or commissions as to any particular underwriter, broker-dealer or agent may be in excess of those customary in the types of transactions involved. In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders.

The securities may be sold in one or more transactions at fixed prices, at prevailing market prices at the time of sale, at varying prices determined at the time of sale or at negotiated prices. These sales may be effected in transactions which may involve crosses or block transactions.

If underwriters are used in an offering of securities, such offered securities may be resold in one or more transactions:

on any national securities exchange or quotation service on which the preferred stock or the common stock may be listed or quoted at the time of sale, including, as of the date of this prospectus, the NASDAQ Capital Market in the case of the common stock;

in the over-the-counter market;

in transactions otherwise than on these exchanges or services or in the over-the-counter market; or

through the writing of options, whether the options are listed on an options exchange or otherwise. Each prospectus supplement will state the terms of the offering, including, but not limited to:

the names of any underwriters, dealers, or agents;

the public offering or purchase price of the securities and the net proceeds that we will receive from the sale;

any underwriting discounts and commissions or other items constituting underwriters' compensation;

any discounts, commissions, or fees allowed or paid to dealers or agents; and

any securities exchange on which the offered securities may be listed.

If we sell securities to underwriters, we will execute an underwriting agreement with them at the time of the sale and will name them in the applicable prospectus supplement. In connection with these sales, the underwriters may be deemed to have received compensation in the form of underwriting discounts and commissions. The underwriters also

may receive commissions from purchasers of securities for whom they may act as agent. Unless we specify otherwise in the applicable prospectus supplement, the underwriters will not be obligated to purchase the securities unless the conditions set forth in the underwriting agreement are satisfied, and if the underwriters purchase any of the securities offered by such prospectus supplement, they will be required to purchase all of such offered securities. The underwriters may acquire the securities for their own account and may resell the securities from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or varying prices determined at the time of sale. The underwriters may sell the securities to or through dealers, and those dealers may receive discounts, concessions, or commissions from the underwriters as well as from the purchasers for whom they may act as agent.

We may designate agents who agree to use their reasonable efforts to solicit purchasers for the period of their appointment or to sell securities on a continuing basis. We may also sell securities directly to one or more purchasers without using underwriters or agents.

- 36 -

Table of Contents

Under agreements entered into with us, underwriters and agents may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution for payments the underwriters or agents may be required to make. The underwriters, agents, and their affiliates may engage in financial or other business transactions with us and our subsidiaries in the ordinary course of business.

The aggregate proceeds to us from the sale of the securities will be the purchase price of the securities less discounts and commissions, if any.

In order to comply with the securities laws of certain states, if applicable, any securities covered by this prospectus must be sold in such jurisdictions only through registered or licensed brokers or dealers. In addition, in certain states securities may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallocate in connection with the offering, creating a short position for their own accounts. In addition, to cover overallocations or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

The applicable prospectus supplement may provide that the original issue date for your securities may be more than three scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the third business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than three scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

In order to comply with the securities laws of some states, if applicable, the shares of common stock offered by this prospectus must be sold in such jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the shares of common stock may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

To the extent required, this prospectus may be amended or supplemented from time to time to describe a specific plan of distribution.

Transfer Agent

The transfer agent and registrar for Agenesis common stock is American Stock Transfer & Trust Company. Its telephone number is (800) 937-5449.

- 37 -

Table of Contents

LEGAL MATTERS

The validity of the securities that may be offered hereby will be passed upon for us by Choate, Hall & Stewart LLP.

- 38 -

Table of Contents

EXPERTS

The consolidated financial statements of Agenus Inc., as of December 31, 2013 and 2012, and for each of the years in the three-year period ended December 31, 2013, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2013 have been incorporated by reference herein and in the registration statement in reliance upon the reports of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

The audited historical financial statements of 4-Antibody AG, incorporated by reference into our Current Report on Form 8-K filed February 13, 2014 (as amended by our Current Report on Form 8-K/A filed April 29, 2014), have been incorporated by reference herein in reliance on the report of Ernst & Young Ltd, independent auditors to 4-Antibody AG, given on the authority of such firm as experts in accounting and auditing.

- 39 -

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION

Agenus Inc. is subject to the information requirements of the Securities Exchange Act of 1934, as amended, and files annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any materials we file with the SEC at the Public Reference Room of the SEC at Room 1580, 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. In addition, we file many of our documents electronically with the SEC, and you may access those documents over the Internet. The SEC maintains a web site that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. The address of the SEC's website is <http://www.sec.gov>. Documents we have filed with the SEC are also available on our website through the investor link at www.agenusbio.com. Information contained on our web site does not constitute a part of this prospectus and is not incorporated by reference herein.

- 40 -

Table of Contents

Shares

Agenus Inc.

Common Stock

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

Jefferies

William Blair

Co-Manager

Oppenheimer & Co.

May , 2015