AGENUS INC
Form S-3
May 09, 2014
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As filed with the Securities and Exchange Commission on May 9, 2014

Registration No. 333-

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

AGENUS INC.

(Exact name of Registrant as specified in its charter)

Delaware	**06-1562417**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**

3 Forbes Road

Lexington, MA 02421

(781) 674-4400

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

Garo H. Armen

Chief Executive Officer and Chairman of the Board

Agenus Inc.

3 Forbes Road

Lexington, MA 02421

(781) 674-4400

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

Copy to:

Gerald E. Quirk, Esq.

Choate, Hall & Stewart LLP

Two International Place

Boston, MA 02110

(617) 248-5000

Approximate date of commencement of proposed sale to the public: From time to time after this registration statement becomes effective.

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

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

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

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

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

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

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

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Share(2)	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, $0.01 par value per share	3,717,117	$2.62	$9,738,846.54	$1,254.36

(1) The Registrant is hereby registering for resale from time to time by the selling stockholders up to 3,717,117 shares of its common stock that were initially issued pursuant to the terms of the Share Exchange Agreement dated as of January 10, 2014 by and among the Registrant, 4-Antibody AG, a joint stock company formed under the laws of Switzerland (4-AB), the shareholders of 4-AB and Vischer AG as Representative, and for the repayment of certain indebtedness owed by 4-AB to the selling stockholders on May 8, 2014. Pursuant to Rule 416 under the Securities Act, this Registration Statement also covers such additional number of shares of common stock that may be issued as a result of stock splits, stock dividends or similar transactions.

(2) Estimated solely for purposes of determining the registration fee pursuant to Rule 457(c) under the Securities Act, based on the average high and low prices per share of the common stock as reported on the Nasdaq Capital Market on May 8, 2014.

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

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The information contained in this prospectus is not complete and may be changed. The selling stockholders named in this prospectus may not sell these securities until the registration statement becomes effective. This prospectus is not an offer to sell these securities, and the selling stockholders named in this prospectus are not soliciting offers to buy these securities in any jurisdiction where the offer for sale is not permitted.

Subject To Completion, Dated May 9, 2014

PROSPECTUS

3,717,117 SHARES OF COMMON STOCK

We have prepared this prospectus to allow certain stockholders, or their pledgees, donees, transferees, distributees, beneficiaries or other successors in interest, to sell from time to time in the future up to 3,717,117 shares of our common stock that they have acquired from us in private placements. Any such stockholders are referred to in this prospectus as the selling stockholders.

We will not receive any proceeds from the sale of these shares. Any of these shares may be sold in public or private transactions at prevailing market prices at the time of sale, at varying prices determined at the time of sale, or at privately negotiated prices. See Plan of Distribution on page 32 of this prospectus. Any selling stockholders will bear all commissions and discounts, if any, attributable to those sales. We will bear all costs, expenses and fees in connection with the registration of the shares.

Our common stock is listed on The NASDAQ Capital Market and trades under the symbol AGEN. On May 8, 2014, the last sale price of our common stock as reported on the NASDAQ Capital Market was $2.49 per share. You are urged to obtain current market quotations for our common stock.

Investing in our securities involves risks. See Risk Factors beginning 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 , 2014.

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You should read this prospectus, including all documents incorporated herein by reference, together with additional information described under Where You Can Find More Information.

You may obtain the information incorporated by reference without charge by following the instructions under Where You Can Find More Information.

We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. The selling stockholders may offer to sell, and seek offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of common stock.

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PROSPECTUS SUMMARY

The following is a summary of selected information contained elsewhere or incorporated by reference in this prospectus. It does not contain all of the information that you should consider before investing in our securities. You should read this entire prospectus carefully, especially the sections entitled Risk Factors and the consolidated financial statements and the notes to the consolidated financial statements incorporated in this prospectus by reference. As used in this prospectus, Agenus, the Company, we, us, and our refer to Agenus Inc. and its consolidated subsidiaries.

Agenus Inc.

Our Business

We are a biopharmaceutical company developing a portfolio of immuno-oncology candidates, including checkpoint modulator antibodies, heat shock protein-based vaccines and saponin 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 Checkpoint Modulator Antibody Programs became part of our portfolio with the acquisition of 4-Antibody AG, a private European-based biopharmaceutical company (4-AB), in February 2014. The Retrocyte Display® Technology Platform is intended to enable, among other things, the rapid generation and optimization of fully human monoclonal antibodies against a broad range of target antigens of interest. We currently have six pre-clinical Checkpoint Modulator Antibody Programs which target GITR, OX40, CTLA-4, PD-1, TIM-3 and LAG-3. We have selected two GITR agonists and one CTLA-4 antagonist to advance into investigational new drug application (IND) enabling development. Although we envision using Retrocyte Display® to drive the discovery of future checkpoint modulator 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 plan to identify development candidates for the other four Checkpoint Modulator Antibody Programs during 2014, in order to be in a position to file INDs on at least four candidates within the next two years.

Within our HSP-Based Platform we are developing our Prophage Series cancer vaccines. Our Prophage Series cancer 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.

Also within our HSP-Based Platform, is HerpV, a recombinant, synthetic vaccine containing multiple antigens derived from the herpes simplex 2 virus. Combining our heat shock protein-based 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. We anticipate reporting additional study results assessing the efficacy of a booster injection of HerpV during the second quarter of 2014. HerpV evokes immune responses to the mix of HSV2 peptides contained in the vaccine in a substantial majority of patients. Our Phase 2 study has shown that HerpV may reduce viral shedding, which has the potential to reduce the incidence and severity of herpetic lesion outbreaks and/or reduce the likelihood of disease transmission. However, 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.

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Within our Saponin Adjuvant Platform is QS-21 Stimulon® adjuvant, or QS-21 Stimulon. QS-21 Stimulon 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 widely studied in 50,000 patients. The key licensees of QS-21 Stimulon are GlaxoSmithKline (GSK) and JANSSEN Alzheimer Immunotherapy (JANSSEN AI). QS-21 Stimulon is currently being studied in approximately 20 vaccine indications, which include GSK s Phase 3 vaccine programs for RTS,S for malaria, MAGE-A3 cancer immunotherapeutic for melanoma and HZ/su for shingles. In addition, JANSSEN AI s QS-21 Stimulon adjuvant-containing vaccine candidate is in Phase 2 trials for the treatment of Alzheimer s disease. If any of our partners products containing QS-21 Stimulon successfully completes clinical development and receives approval for commercial sale, we are generally entitled to receive 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. In April 2014, we entered into a collaboration and license agreement with Merck to discover and optimize fully human antibodies against two undisclosed Merck checkpoint targets using the Retrocyte Display® Technology Platform. Merck will be responsible for the clinical development and commercialization of candidates generated under the collaboration and we are eligible to receive potential payments associated with the completion of certain clinical, regulatory and commercial milestones as well as royalty payments on worldwide product sales.

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 March 31, 2014, plus potential proceeds from 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 (i) our Retrocyte Display® Technology Platform, Checkpoint Modulator Antibody Programs, HerpV and the Prophage Series vaccines, (ii) vaccines containing QS-21 Stimulon under development by our licensees, and/or (iii) the 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.

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.

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The Offering

Common Stock offered by the selling stockholders	3,717,117 shares
Use of Proceeds	We will not receive any proceeds from the sale of shares in this offering
Nasdaq Capital Market Symbol	AGEN

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below in addition to the other information included or incorporated by reference in this prospectus before purchasing our common stock. If any of the following risks actually occurs, our business, financial condition or results of operations would likely suffer, possibly materially. In that case, the trading price of our common stock could fall, and you may lose all or part of the money you paid to buy our common stock.

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, 2013, 2012, and 2011, were $30.1 million, $11.3 million, and $23.3 million, respectively. During the quarter ended March 31, 2014, we generated net loss of $357,513 due primarily to a fair value adjustment to our contingent royalty obligation at March 31, 2014.

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, and such losses may increase as a result of our acquisition of 4-AB. 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 vaccines containing QS-21 Stimulon, our Prophage Series vaccines and our other product candidates. From our inception through March 31, 2014, we have incurred net losses totaling $649.2 million.

On March 31, 2014, we had $73.5 million in cash and cash equivalents. We believe that, based on our current plans and activities, our working capital resources at March 31, 2014, and potential proceeds from 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 funds although additional funding may not be available on favorable terms, or at all. For the quarter ended March 31, 2014, our average monthly cash used in operating activities was approximately $3.4 million.

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, 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 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:

- the number and characteristics of the product candidates we pursue;

the scope, progress, results and costs of researching and developing our future product candidates, and conducting preclinical and clinical trials;

the timing of, and the costs involved in, obtaining regulatory approvals for our and our licensees product candidates;

the cost of manufacturing;

our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;

the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing our intellectual property rights;

the costs associated with any successful commercial operations; and

the timing, receipt and amount of sales of, or royalties on, our future products, if any.

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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.

Certain of our outstanding debt instruments contain significant restrictive and affirmative covenants and we may not be able to make interest or principal payments when due or otherwise remain in compliance with their terms.

In April 2013 we exchanged our 8% senior secured convertible notes due August 2014 (the 2006 Notes), including accrued and unpaid interest, for $10.0 million in cash, 2,500,000 shares of our common stock, a revenue interest in certain QS-21 Stimulon partnered programs and a royalty interest in HerpV. The $10.0 million cash payment was financed by entering into a Loan and Security Agreement with Silicon Valley Bank for a $5.0 million loan that bears interest at 6.75% annually (the SVB Loan), and a Note Purchase Agreement with various investors to issue senior subordinated notes in the aggregate principal amount of $5.0 million with annual interest at 10% (the Subordinated Notes). The SVB Loan is payable in equal monthly installments of approximately $278,000 until April 2015. The Subordinated Notes are due in April 2015.

The SVB Loan is secured by a lien against substantially all of our assets as well as the assets of our subsidiary Antigenics Inc., and contains, among other things, a number of restrictions and covenants that limit our ability to:

- incur certain additional indebtedness;
- make certain investments;
- pay dividends other than dividends required pursuant to pre-existing commitments;
- make payments on subordinated indebtedness other than regularly scheduled payments of interest;
- create certain liens;
- consolidate, merge, sell or otherwise dispose of our assets; and/or
- change our line of business.

The SVB Loan also specifies a number of events of default (some of which are subject to applicable cure periods), including, among other things:

- covenant defaults;

other non-payment defaults;

bankruptcy;

certain penalties and judgments from a governmental authority;

cross-defaults in respect of indebtedness over $50,000; and

insolvency defaults.

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Additionally, any material adverse change with respect to us or Antigenics Inc., constitutes an event of default. Upon the occurrence of an event of default under the SVB Loan, subject to cure periods in certain circumstances, the Lender may declare all amounts outstanding to be immediately due and payable and may foreclose upon our assets that secure the SVB Loan. During the continuance of an event of default which does not accelerate the maturity of the SVB Loan, interest will accrue at a default rate equal to the otherwise applicable rate plus 5%. We may prepay the SVB Loan at any time, in full, subject to certain notice requirement and a prepayment premium equal to 4% of the outstanding principal amount of the SVB Loan.

The Subordinated Notes also include default provisions which allow for the acceleration of the principal payment of the 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 Subordinated Notes, default on other indebtedness with an aggregate principal balance of $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 $5 million if such amount will not be covered by third-party insurance.

If we default on the SVB Loan or the Subordinated Notes and the repayment of such indebtedness is accelerated, our liquidity will 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 are not able to generate sufficient cash flow from operations in the future to service our indebtedness, we may be required, among other things, to:

seek additional financing in the debt or equity markets;

refinance or restructure all or a portion of our indebtedness;

sell, out-license, or otherwise dispose of assets; and/or

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 economically favorable terms, if at all.

Other than for the year ended December 31, 2012, we have had negative cash flows from operations. The net cash provided by operations of $1.0 million for the year ended December 31, 2012 primarily resulted from one-time payments received under amended license agreements and therefore our net cash provided by operations for the year ended December 31, 2012 is not indicative of future results. For the three months ended March 31, 2014 and for the years ended December 31, 2013, and 2011, net cash used in operating activities was $10.1 million, $19.5 million, and $16.2 million, respectively.

We may fail to realize the benefits we expect to realize as a result of the acquisition of 4-AB and/or we may suffer a loss in productivity as a result of the integration process.

The long-term success of the acquisition of 4-AB will depend, in part, on our ability to realize the anticipated synergies, business opportunities and growth prospects from combining the businesses of Agenus and 4-AB. We may never realize these anticipated synergies, business opportunities and growth prospects. We might

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experience increased competition that limits our ability to expand our business, and we might not be able to capitalize on expected business opportunities, including maintaining current collaboration relationships and advancing the development of the 4-AB Checkpoint Modulator Antibody Programs. Moreover, assumptions underlying estimates of expected costs as a result of the acquisition may be inaccurate, and general industry and business conditions might deteriorate. If any of these factors limit our ability to integrate the operations of Agenus and 4-AB successfully or on a timely basis, or to develop the business opportunities that we expect to realize from the acquisition of 4-AB, the expectations of future results of operations, including certain cost savings and synergies expected to result from the acquisition, might not be met.

In addition, integrating operations is complex and requires significant efforts and expenditures for us and 4-AB. During or as a result of the integration process, employees might leave, be terminated, or have decreased productivity, and our management might have its attention diverted from core business objectives while trying to integrate operations and corporate and administrative infrastructures.

We may not receive anticipated QS-21 Stimulon revenues from our licensees.

With the exception of our HerpV program, we currently rely upon and expect to continue to rely upon third party licensees, particularly GlaxoSmithKline (GSK) and JANSSEN Alzheimer Immunotherapy (JANSSEN AI), to develop, test, market and manufacture vaccines that utilize our QS-21 Stimulon adjuvant. We expect that we will rely on similar relationships if we develop new adjuvants in our Saponin Adjuvant Platform.

In return for rights to use QS-21 Stimulon, our licensees have generally agreed to pay us license fees, milestone payments and royalties on product sales for a minimum of 10 years after commercial launch, with some exceptions. 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. Clinical trials being conducted by our licensees, including those being conducted by GSK and JANSSEN AI, 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 they announced the Phase 3 trial of their MAGE-A3 cancer immunotherapeutic in melanoma missed its first co-primary endpoint and the study would continue until completion of its second co-primary endpoint, which is expected 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. In the event that our licensees develop vaccines using QS-21 Stimulon, there is no guarantee that these products will obtain regulatory approval or, if so approved, will generate significant royalties, if any, or that we will be able to collect royalties in the future.

In addition, where we had previously supplied GSK and JANSSEN AI with all their requirements of QS-21 Stimulon, we have amended our agreements so that they are permitted to manufacture their own QS-21 Stimulon. We are unable to predict what amount of QS-21 Stimulon, if any, will be purchased from us by other licensees or collaborators in the future. Any inability to receive anticipated QS-21 Stimulon revenues would have a material adverse effect on our business, financial condition and results of operations.

In connection with the exchange of our 2006 Notes, we entered into a Revenue Interests Assignment Agreement with the holders of the 2006 Notes. This agreement granted these holders a contractual right to the proceeds of 20% of our revenue interests from QS-21 Stimulon partnered programs and a 0.5% royalty on net sales of HerpV. Due to uncertainties surrounding the future revenue stream generated from our licensees, we are unable to predict the precise dollar value reduction in revenue that will result from this agreement to pay the 2006 Note holders their share of the proceeds from QS-21 Stimulon and HerpV programs. Any reduction in revenues generated from QS-21 Stimulon

could have a material adverse effect on our business, financial condition and results of operations.

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Our HerpV therapeutic vaccine candidate is in early stage development and we may not be able to successfully develop this candidate.

Based on the results of our Phase 1 clinical trial of HerpV, which includes QS-21 Stimulon, we advanced this product candidate into a Phase 2 trial that measured the effect of vaccination on viral shedding in individuals infected with HSV-2 (genital herpes). In November 2013, we announced that the Phase 2 trial met its primary endpoint, a statistically significant reduction in viral shedding. Additional study results, including booster and immune response data, are expected during the first half of 2014. The findings to date from our clinical trials, while positive, were limited in size and scope and may be insufficient to attract partnering arrangements or warrant further development of the HerpV program. In addition, even if we proceed with further HerpV development, there is no guarantee that future clinical trials will be successful, that a reduction in viral shedding will translate into clinical benefit, or that the safety profile will be considered acceptable. In addition, the success of future clinical trials, if any, is dependent on, upon other things, maintaining sufficient supply of the required investigational materials, enrolling sufficient patients and the adherence of these patients to the study protocol. Furthermore, it is possible that research and discoveries by others will render our product candidate obsolete or noncompetitive.

We may not be able to advance clinical development or commercialize Prophage Series Vaccines.

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 has not been successful by us or NewVac LLC (NewVac) our licensee, for Oncophage® in the Russian Federation and certain other CIS countries. Due to our limited resources or a shift in corporate priorities, we may be unable or limited in our ability to support on-going clinical studies with Prophage Series vaccines, or perform additional ones.

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 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 Avastin® (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 NCI. 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 Avastin for the treatment of recurrent glioma could exacerbate enrollment issues and/or render the trial design impractical. In January 2014 we announced the initiation of a randomized Phase 2 trial with Prophage Series vaccine and Bristol-Myers Squibb s Yervoy® (ipilimumab), for the treatment of Stage III and IV metastatic melanoma. While we believe the combination has the potential to trigger a more effective immune response against the tumor than Yervoy alone, there is no guarantee that this trial will be completed or that it will yield useful translational and/or efficacy data. This study is being sponsored by an investigator at the University of Texas and, although the investigator-held investigational new drug application (IND) has been activated to allow initiation of the trial, patient enrollment has not yet been initiated.

If we or our licensee are unable to purify heat shock proteins we may have difficulty successfully initiating or completing clinical trials or supporting commercial sales of Prophage Series vaccines.

The successful development and commercialization of Prophage Series vaccines for a particular cancer depends in part on the ability of NewVac to purify sufficient heat shock proteins from that type of cancer. If we or NewVac have difficulties in purifying heat shock proteins for a sufficiently large number of patients in clinical trials, we may experience enrollment delays and/or lower the probability of a successful analysis of the data from clinical trials. We have successfully manufactured product across many different cancer types, however, the success

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rate per indication has varied. We have evolved our manufacturing processes to better accommodate a wider range of tumor types. Our current manufacturing technologies have been successful in manufacturing product from approximately 92% of the RCC tumors received and approximately 85% of the tumors received from patients enrolled in Phase 2 clinical trials for the treatment of recurrent glioma. In addition, we may encounter problems with other types of cancer or patients if we expand our research. If we cannot overcome these problems, the number of patients or cancer types that our heat shock protein-based product candidates could treat would be limited. In addition, if we commercialize our heat shock protein-based product candidates, we may not be able to replicate past manufacturing success rates and we may face claims from patients for whom we are unable to produce a vaccine.

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.

We currently manufacture our Prophage Series vaccines in our Lexington, MA facility. There is no guarantee that we will be able to meet future manufacturing demand for Prophage Series vaccines, and a failure to do so could cause a delay or cessation in the further development of our Prophage Series vaccine programs. Manufacturing of Prophage Series vaccines is complex, and various factors could cause delays or an inability to supply 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 key QS-21 Stimulon licensees, GSK and JANSSEN AI, 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, 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.

The Checkpoint Modulator Antibody Programs, new to our business through the acquisition of 4-AB, will require substantial manufacturing development and investment to develop. The Checkpoint Modulator Antibody Programs are preclinical, 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 Checkpoint Modulator Antibody Programs and we currently rely on consultants and advisors to advance these operations. We are in the process of identifying a contract manufacturers (CMO) for our Checkpoint Modulator Antibody Programs. During the early development stages of the Checkpoint Modulator Antibody programs, we will likely be using only one CMO, and will not have a backup manufacturer in place. In the future, we may need to secure additional CMOs and we will 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 Checkpoint Modulator Antibody programs require progressively larger production capabilities, our options for 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 may elect to alter our manufacturing strategy and hire CMOs to manufacture our internally manufactured products, which would require additional time and resources to identify suitable CMOs and transfer the technology and systems. Such an effort could divert resources away from the Checkpoint Modulator Antibody programs and lead to delays in the development of product candidates. In addition, 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.

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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, preclinical 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.

There are a limited number of CMOs or suppliers that are capable of manufacturing our product candidates or the materials used in their manufacture. If we are unable to do so ourselves or to arrange for third-party manufacturing or supply of these product candidates or materials, or to do so on commercially reasonable terms, we may not be able to complete development of these product candidates or commercialize them ourselves or through our collaborative partners or licensees. 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 ongoing 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 in the past, and may continue to pursue pathways to develop and commercialize our product candidates in non-U.S. jurisdictions. For example, our Oncophage® vaccine is approved for sale in Russia for the treatment of kidney cancer patients at intermediate risk for disease recurrence, and we have partnered to commercialize this product in the Russian Federation with NewVac, who has been unsuccessful to date in doing so. In addition, due to the acquisition of 4-AB, we now have research and development operations in Switzerland and Germany. 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. 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 and Risk Factors - We may fail to realize the benefits we expect to realize as a result of the acquisition of 4-AB or suffer a loss of productivity as a result of the integration process.

If we, or our licensees, fail to obtain market demand or adequate levels of reimbursement for our product candidates, there may be no commercial or partnering opportunities for these products, or such opportunities may be significantly limited.

We or our current and future strategic alliance partners, if any, may be unable to dedicate sufficient resources to the commercialization of our current and future products and product candidates or may otherwise fail in their commercialization due to factors beyond our control. Although our Oncophage® vaccine is approved for sale in Russia for the treatment of kidney cancer patients at intermediate risk for disease recurrence, our licensee,

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NewVac, has been unsuccessful in securing reimbursement or market demand for this product, and it is unlikely that it will be able to do so. In addition, as we advance our Checkpoint Modulator Antibody Programs, we will be competing in a very crowded industry. If products that compete directly or indirectly with our products or product candidates prove superior to existing antibodies, market demand for our products or product candidates could be hampered or non-existent. We and our strategic partners, if any, will face competition from other products currently approved or that will be approved in the future for the same therapeutic indications.

In addition, public and private insurance programs may determine that they will not cover our product candidates or the product candidates of our licensees. Government-sponsored health care systems typically pay a substantial share of health care costs, and they may regulate reimbursement levels of products to control costs. If we or our licensees are unsuccessful in obtaining substantial reimbursement for our product candidates from national or regional funds, we will have to rely on private-pay, which may delay or prevent commercialization and/or partnering efforts. We, or our licensees, may not be able to obtain health insurance coverage of our product candidates, and if coverage is obtained, it may be substantially delayed, or there may be significant restrictions on the circumstances in which the products would be reimbursed. We are unable to predict what impact any future regulation or third-party payer initiatives relating to reimbursement will have on any potential future sales for our product candidates.

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:

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

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

Competitive products in our HerpV program include Valtrex (GSK) and Famvir (Novartis), which are small molecule drugs marketed for treatment of genital herpes. Other companies are engaged in research and/or clinical development for vaccines for treatment of genital herpes including Genocea and Vical. AiCuris Gmbh is engaged in clinical research of a small molecule drug for treatment of genital herpes and has completed a Phase 2 trial.

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

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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 with our ability to do future partnering and licensing deals with QS-21 Stimulon.

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 Avastin and Eisai and Arbor Pharmaceuticals market Gliadel, both for treatment of recurrent glioma. 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 Temodar 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 Innocell Corp (Immuncell-LC), ImmunoCellular Therapeutics (ICT-107), Northwest Biotherapeutics (DC-Vax), Immatics (IMA-950), Activartis Biotech (GBM-Vax) and Celldex (CDX-110). Celldex is also currently developing a vaccine candidate for recurrent glioma. Other companies may begin such development as well.

If vaccines from our Prophage Series 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.

We have six preclinical Checkpoint Modulator Antibody Programs that have been commenced by 4-AB, our wholly-owned subsidiary. We are aware of several large companies that have antibody-based products on the market or in clinical development that are directed to the same biological target as some of these programs, including Bristol-Myers Squibb, which markets ipilimumab, an anti-CTLA-4 antibody, and has an anti-PD1 antibody in development, Medimmune, which has anti-CTLA-4, OX-40 and PD1 antibodies in development, Merck and Curetech, which each has an anti-PDI antibody in development, and Pfizer, which has an anti-CTLA-4 antibody in development. Tesaro also has antibody programs targeting PD-1, TIM-3 and LAG-3 and these include both monospecific and dual reactive antibody drug candidates.

Our future growth depends on our ability to successfully identify, develop, acquire or in-license 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:

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

incurrence of substantial debt or dilutive issuances of securities to pay for development, acquisition or in-licensing of new products;

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disruption of our business and diversion of our management s time and attention;

higher than expected development, acquisition or in-license and integration costs;

exposure to unknown liabilities;

difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;

inability to retain key employees of any acquired businesses;

difficulty in managing multiple product development programs; and

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.

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 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, we have not entered into a substantial agreement relating to the potential development or commercialization of any of our Prophage Series vaccines other than the agreement with NewVac to which we granted an exclusive license to manufacture, market and sell Oncophage as well as pursue a development program in the Russian Federation and certain other CIS countries.

To date, the NewVac arrangement has not provided substantial benefit to us, and it is unlikely that it will. NewVac has experienced challenges establishing manufacturing capabilities and securing government reimbursement, and has not met certain milestones set within the license agreement. 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.

We would consider license and/or co-development opportunities to advance HerpV and antibody candidates derived from the Retrocyte Display® Technology Platform, as well as collaborations to develop antibodies derived from the Retrocyte Display® Technology Platform against targets of interest. However, collaborative partners or licensees may defer discussions until these assets are further developed or validated, or they may not engage in such discussions on terms acceptable to us or at all.

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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, preclinical and clinical testing, completing regulatory applications, and commercializing product candidates. For example, development of Prophage Series vaccine for the treatment of patients with recurrent glioma is dependent, in large part, on the efforts of the Alliance for Clinical Trials in Oncology, a National Cancer Institute cooperative group, which is sponsoring a Phase 2 clinical trial of this product candidate in this indication. 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, other than HerpV, 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 commercializing product candidates. We have granted NewVac an exclusive license to manufacture, market and sell Oncophage® in the Russian Federation and certain other CIS countries. NewVac has faced challenges establishing manufacturing capabilities and securing government reimbursement, which has impacted its ability to commercialize the product in the licensed territory. NewVac may terminate this agreement at any time without cause and it is expected to otherwise terminate in December 2014. We do not expect to receive financial or other benefits from our relationship with NewVac or the sale of Oncophage® in the Russian Federation or CIS countries.

In addition, our research, development, and commercialization efforts with respect to antibody candidates from the Retrocyte Display® Technology Platform include the participation of institutional and corporate collaborators. For example, 4-AB has collaborative arrangements with Ludwig Cancer Research and Brazil-based Recepta Biopharma SA, among others. If we are not able to 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.

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.

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We are highly reliant on our Chief Executive 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.

Garo H. Armen, Ph.D., the Chairman of our Board of Directors and our Chief Executive Officer, co-founded the Company in 1994, and has been, and continues to be, integral to building our company and developing our technology. If Dr. Armen is unable or unwilling to continue his relationship with Agenus, our business may be adversely impacted.

Effective December 1, 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. Dr. Armen plays an important role in our day-to-day activities. We do not carry key employee insurance policies for Dr. Armen or any other employee.

We also rely on a small staff of highly trained and experienced senior management and scientific, administrative and operations personnel and consultants to conduct our business. Reductions in our staffing levels have eliminated redundancies in key capabilities and skill sets among our full time staff and required us to rely more heavily on outside consultants and third parties. In addition, if in the future we need to perform sales, marketing and distribution functions for commercial and/or international operations, we will need to recruit experienced personnel and/or engage external consultants incurring significant expenditures.

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 preclinical testing and the process of obtaining and maintaining regulatory approvals for new therapeutic products, is lengthy, expensive, and uncertain. As of March 31, 2014, we have spent approximately 19 years and $305.3 million on our research and development program in heat shock protein-based vaccines for cancer. It also can vary substantially based on the type, complexity, and novelty of the product. We must provide regulatory authorities with manufacturing, product characterization, and preclinical 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 preclinical 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 preclinical 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. Preclinical and clinical data can be interpreted in different ways, which could delay, limit, or prevent regulatory approval. Negative or inconclusive results from a preclinical 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 preclinical 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

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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:

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