AGENUS INC
Form 424B3
March 06, 2012
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**Filed Pursuant to Rule 424(b)(3) and Rule 424(c)**

**Registration No. 333-149116**

**March 6, 2012**

**PROSPECTUS SUPPLEMENT NO. 56**

**2,902,900 SHARES OF COMMON STOCK**

**AGENUS INC.**

This prospectus supplement amends the prospectus dated March 16, 2009 (as supplemented on April 15, 2009, April 17, 2009, April 22, 2009, April 27, 2009, May 4, 2009, May 11, 2009, May 27, 2009, June 4, 2009, June 8, 2009, June 9, 2009, June 11, 2009, June 15, 2009, July 7, 2009, July 15, 2009, August 3, 2009, August 5, 2009, September 11, 2009, September 18, 2009, November 12, 2009, January 5, 2010, March 1, 2010, March 25, 2010, April 26, 2010, May 11, 2010, May 18, 2010, July 23, 2010, August 9, 2010, August 25, 2010, November 3, 2010, November 10, 2010, December 30, 2010, January 7, 2011, January 14, 2011, January 28, 2011, March 1, 2011, March 8, 2011, March 18, 2011, April 18, 2011, May 5, 2011, May 9, 2011, June 8, 2011, June 17, 2011, August 8, 2011, August 16, 2011, September 7, 2011, September 27, 2011, September 30, 2011, October 11, 2011, October 20, 2011, November 7, 2011, November 17, 2011, December 12, 2011, December 21, 2011, and March 5, 2012) to allow certain stockholders or their pledgees, donees, transferees, or other successors in interest (the Selling Stockholders ), to sell, from time to time, up to 1,451,450 shares of our common stock, which they have acquired in a private placement in the United States, and up to 1,451,450 shares of our common stock issuable upon the exercise of warrants which are held by the Selling Stockholders named in the prospectus.

We would not receive any proceeds from any such sale of these shares. To the extent any of the warrants are exercised for cash, if at all, we will receive the exercise price for those warrants.

This prospectus supplement is being filed to include the information set forth in the Annual Report on Form 10-K filed on March 6, 2012, which is set forth below. This prospectus supplement should be read in conjunction with the prospectus dated March 16, 2009, Prospectus Supplement No. 1 dated April 15, 2009, Prospectus Supplement No. 2 dated April 17, 2009, Prospectus Supplement No. 3 dated April 22, 2009, Prospectus Supplement No. 4 dated April 27, 2009, Prospectus Supplement No. 5 dated May 4, 2009, Prospectus Supplement No. 6 dated May 11, 2009, Prospectus Supplement No. 7 dated May 27, 2009, Prospectus Supplement No. 8 dated June 4, 2009, Prospectus Supplement No. 9 dated June 8, 2009, Prospectus Supplement No. 10 dated June 9, 2009, Prospectus Supplement No. 11 dated June 11, 2009, Prospectus Supplement No. 12 dated June 15, 2009, Prospectus Supplement No. 13 dated July 7, 2009, Prospectus Supplement No. 14 dated July 15, 2009, Prospectus Supplement No. 15 dated August 3, 2009, Prospectus Supplement No. 16 dated August 5, 2009, Prospectus Supplement No. 17 dated September 11, 2009, Prospectus Supplement No. 18 dated September 18, 2009, Prospectus Supplement No. 19 dated November 12, 2009, Prospectus Supplement No. 20 dated January 5, 2010, Prospectus Supplement No. 21 dated March 1, 2010, Prospectus Supplement No. 23 dated March 25, 2010, Prospectus Supplement No. 24 dated April 26, 2010, Prospectus Supplement No. 25 dated May 11, 2010, Prospectus Supplement No. 26 dated May 18, 2010, Prospectus Supplement No. 27 dated July 23, 2010, Prospectus Supplement No. 28 dated August 9, 2010, Prospectus Supplement No. 29 dated August 25, 2010, Prospectus Supplement No. 30 dated November 3, 2010, Prospectus Supplement No. 31 dated November 10, 2010, Prospectus Supplement No. 32 dated December 30, 2010, Prospectus Supplement No. 33 dated January 7, 2011, Prospectus Supplement No. 34 dated January 14, 2011, Prospectus Supplement No. 35 dated January 28, 2011, Prospectus Supplement No. 36 dated March 1, 2011, Prospectus Supplement No. 37 dated March 8, 2011, Prospectus Supplement No. 38 dated March 18, 2011, Prospectus Supplement No. 39 dated April 18, 2011, Prospectus Supplement No. 40 dated May 5, 2011, Prospectus Supplement No. 41 dated May 9, 2011, Prospectus Supplement No. 42 dated June 8, 2011, Prospectus Supplement No. 43 dated June 17, 2011, Prospectus Supplement No. 44 dated August 8, 2011, Prospectus Supplement No. 45 dated August 16, 2011, Prospectus Supplement No. 46 dated September 7, 2011, Prospectus Supplement No. 47 dated September 27, 2011, Prospectus Supplement No. 48 dated September 30, 2011, Prospectus Supplement No. 49 dated October 11, 2011, Prospectus Supplement No. 50 dated October 20, 2011, Prospectus Supplement No. 51 dated November 7, 2011, Prospectus Supplement No. 52 dated November 17, 2011, Prospectus Supplement No. 53 dated December 12, 2011, Prospectus Supplement No. 54 dated December 21, 2011, and Prospectus Supplement No. 55 dated March 5, 2012, which are to be delivered with this prospectus supplement.

Our common stock is quoted on The NASDAQ Capital Market ( NASDAQ ) under the ticker symbol AGEN. On March 2, 2012, the last reported closing price per share of our common stock was $3.23 per share.

**Investing in our securities involves a high degree of risk. Before investing in any of our securities, you should read the discussion of material risks in investing in our common stock. See Risk Factors on page 1 of the 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 SUPPLEMENT NO. 56 IS MARCH 6, 2012**

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# UNITED STATES

# SECURITIES AND EXCHANGE COMMISSION

**Washington, D.C. 20549**

# Form 10-K

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2011

or

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File Number: 000-29089

# 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 No.)*** |

**3 Forbes Road, Lexington, Massachusetts 02421**

**(Address of principal executive offices, including zip code)**

**Registrant s telephone number, including area code:**

**(781) 674-4400**

**Securities registered pursuant to Section 12(b) of the Act:**

| **Common Stock, $.01 Par Value** | **The NASDAQ Capital Market** |
|---|---|
| ***(Title of each class)*** | ***(Name of each exchange on which registered)*** |

**Securities registered pursuant to Section 12(g) of the Act:**

**None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No þ

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No þ

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes þ No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulations S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). þ

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. þ

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

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

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

The aggregate market value of voting stock held by non-affiliates of the registrant as of June 30, 2011 was: $75.9 million. There were 22,492,667 shares of the registrant s Common Stock outstanding as of February 24, 2012.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the definitive proxy statement for the registrant s 2012 Annual Meeting of Stockholders, which definitive proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the registrant s fiscal year end of December 31, 2011, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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**Note Regarding Forward-Looking Statements**

This Annual Report on Form 10-K and other written and oral statements the Company makes 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, intend, plan, believe, will, potential, opportunity, future and other words and terms of similar meaning and expression in connection w 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. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly under Part I-Item 1A. Risk Factors, that we believe could cause actual results to differ materially from any forward-looking statement.

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.

We have included more detailed descriptions of these risks and uncertainties and other risks and uncertainties applicable to our business in Part I-Item 1A. Risk Factors of this Annual Report on Form 10-K. We encourage you to read those descriptions carefully. We caution investors not to place significant reliance on forward-looking statements contained in this document; such statements need to be evaluated in light of all the information contained in this document. Furthermore, the statements speak only as of the date of this document, and we undertake no obligation to update or revise these statements.



**Reverse Stock Split** Except as otherwise indicated, information in this Annual Report on Form 10-K reflects the one-for-six reverse stock split of our common stock effected on October 3, 2011.

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**PART I**

**Item 1.** ***Business***

**Our Business**

***Overview***

Agenus Inc., including its subsidiaries, referred to in this Annual Report on Form 10-K as Agenus, the Company, we, us, and our, is a biotechnology company focused on the development and commercialization of technologies to treat cancers and infectious diseases. Our core technology portfolio consists of our Saponin Platform (based on our saponin adjuvant based technologies) and our Heat Shock Protein ( HSP ) Platform (based on our HSP based technologies).

Some of our key candidates from these technology platforms are highlighted below:

QS-21 Stimulon® adjuvant ( QS-21 ): QS-21, from our Saponin Platform, is an adjuvant, or a substance added to a vaccine or other immunotherapy that is intended to enhance immune response. The key licensees of QS-21 are GlaxoSmithKline ( GSK ) and JANSSEN Alzheimer Immunotherapy ( JANSSEN AI ). There are approximately 15 vaccines containing QS-21 in clinical development by our licensees, including a total of four in Phase 3 testing for malaria, melanoma, non-small cell lung cancer and shingles. The first products containing QS-21 are anticipated to be launched in the 2013-2014 timeframe, and we are generally entitled to royalties for at least 10 years post-launch. However, there is no guarantee that we will be able to collect royalties in the future. The pipeline of product candidates containing QS-21 is extraordinarily diverse, encompassing prophylactic as well as therapeutic vaccines for infectious diseases, multiple cancer types, and Alzheimer s disease. We do not incur clinical development costs for these products.

The Prophage Series vaccines: The Prophage Series vaccines are a patient specific application of our HSP Platform. We believe that the collective results from our clinical trials to date with product candidates from the Prophage Series indicate a favorable safety profile and signals of efficacy in multiple cancer types. Although promising results have been observed to date, there can be no assurances that we will successfully complete all clinical trials or obtain regulatory approvals for these products. The Prophage Series vaccine R-100 is referred to as Oncophage® vaccine (vitespen) and is approved in Russia for the treatment of renal cell carcinoma ( RCC ; kidney cancer) in patients at intermediate risk of recurrence. In a registry following patients from a large randomized Phase 3 trial in non-metastatic RCC, patients at intermediate risk of recurrence who were in the treatment arm and received Prophage Series R-100, demonstrated an approximately 46 percent lower risk of death compared with those in the control arm (n = 362; $P < 0.05$; hazard ratio = 0.54). In December 2011, we secured a local partner for Oncophage when we granted NewVac LLC (a subsidiary of ChemRar Ventures LLC, NewVac ) 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. In addition, Phase 2 trials are underway in the United States testing the Prophage Series vaccine candidates G-100 and G-200 in newly diagnosed and recurrent glioma, respectively.

HerpV: Also derived from our HSP Platform technologies, HerpV is a recombinantly (off-the-shelf) and synthetically produced therapeutic vaccine candidate for the treatment of genital herpes. It has completed Phase 1 testing, where it was shown to elicit both CD4 and CD8 positive T cell responses a first of its kind finding in genital herpes treatment. Because the product contains multiple antigens derived from the herpes simplex 2 virus (HSV-2), it may be applicable to a broader patient population and may have potential in managing outbreaks and disease transmission. We consider this to be a platform technology, since with the integration of heat shock proteins with antigenic peptides we could potentially create therapeutic vaccines for many infectious diseases. We plan to initiate a Phase 2 trial during the second half of 2012.

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In addition to our internal development efforts, we continue to pursue partnering opportunities. We are seeking partners for select products in our portfolio, which include the Prophage G-Series vaccine candidates, G-100 and G-200, QS-21 and HerpV. We are also exploring in-licensing opportunities. Our business activities have included product research and development, intellectual property prosecution, manufacturing, regulatory and clinical affairs, corporate finance and development, market development, business development, and support of our collaborations. Research and development expenses for the years ended December 31, 2011, 2010, and 2009, were $11.0 million, $12.9 million, and $16.9 million, respectively.

Our common stock is currently listed on The Nasdaq Capital Market ( Nasdaq ) under the symbol AGEN . In April 2009, we moved from The Nasdaq Global Market to The Nasdaq Capital Market as part of our plan to regain compliance with minimum market value requirements. On March 3, 2011, we were notified by the Listing Qualifications Staff of Nasdaq (the Staff ) that we were not in compliance with the minimum bid price requirement set forth in Nasdaq Marketplace Rule 5550(a)(2) (the Bid Price Requirement ) because the bid price for our common stock had closed below the minimum $1.00 per share requirement for 30 consecutive business days. Effective October 3, 2011, our certificate of incorporation was amended to effect a reverse stock split of our common stock on the basis of one post-split share for every six pre-split shares to, in part, regain compliance with the Bid Price Requirement. On October 17, 2011, we received notice from the Nasdaq Listing Qualifications Panel (the Panel ) that we had regained compliance with the Bid Price Requirement and otherwise satisfied all requirements for continued listing on Nasdaq.

**Our Products and Technologies Under Development**

**QS-21**

QS-21 Stimulon® adjuvant, from our Saponin Platform, is an adjuvant, or a substance added to a vaccine or other immunotherapy that is intended to enhance immune response. The key licensees of QS-21 are GSK and JANSSEN AI. There are approximately 15 vaccines containing QS-21 in clinical development, including a total of four in Phase 3 testing for malaria, melanoma, non-small cell lung cancer and shingles. Assuming regulatory approval, the first products containing QS-21 are anticipated to be launched in the early 2013-2014 timeframe. The pipeline of product candidates containing QS-21 is diverse, encompassing prophylactic as well as therapeutic vaccines for infectious diseases, multiple cancer types, and Alzheimer s disease. The Company does not incur clinical development costs for these products.

QS-21 is best known for its ability to stimulate antibody, or humoral, immune response, and has also been shown to activate cellular immunity. A natural product, QS-21 is a triterpene glycoside, or saponin, purified from the bark of a South American tree called Quillaja saponaria. It is sufficiently characterized with a known molecular structure, thus distinguishing it from other adjuvant candidates, which are typically emulsions, polymers, or biologicals. QS-21 has been tested in approximately 185 clinical trials involving, in the aggregate, over 40,000 subjects in a variety of cancer indications, infectious diseases, and other disorders. These studies have been carried out by academic institutions and pharmaceutical companies in the United States and internationally. A number of these studies have shown QS-21 to be significantly more effective in stimulating antibody responses than aluminum hydroxide or aluminum phosphate, the adjuvants most commonly used in approved vaccines in the United States today.

***Partnered QS-21 Programs***

A number of pharmaceutical and biotechnology companies have licensed QS-21 from us for use in vaccines to treat a wide variety of human diseases. Companies with QS-21 programs include GSK, and JANSSEN AI. In return for rights to use QS-21, these companies have generally agreed to pay us license fees, manufacturing payments, milestone payments, and royalties on product sales for a minimum of 10 years after commercial launch. In addition to our corporate licensing arrangements, we have developed a number of academic collaborations to test new vaccine concepts and products containing QS-21.

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*GSK*. In July 2006, we entered into a license agreement and a supply agreement with GSK for the use of QS-21. On January 16, 2009, we entered into an Amended and Restated Manufacturing Technology Transfer and Supply Agreement (the Amended GSK supply agreement ) under which GSK has the right to manufacture all of its requirements of commercial grade QS-21. GSK is obligated to supply us (or our affiliates, licensees, or customers) certain quantities of commercial grade QS-21 for a stated period of time. On March 2, 2012 we entered into a First Right to Negotiate and Amendment Agreement amending the license agreement and Amended GSK supply agreement to clarify and include additional rights for the use of QS-21. In addition, we agreed to grant GSK the first right to negotiate for the purchase of the company or certain of our assets. The first right to negotiate will expire after five years. As consideration for entering into this agreement, GSK is obligated to pay us an upfront, non-refundable payment of $9.0 million, $2.5 million of which is creditable toward future royalty payments. In addition, as of December 31, 2011, we have received $10.5 million of a potential $15.3 million in upfront and milestone payments related to these agreements (excluding the $9.0 million upfront consideration due). We are entitled to receive low single-digit royalties on net sales for a period of 7-10 years after the first commercial sale of a resulting GSK product. The agreements may be terminated by either party upon a material breach if the breach is not cured within the time specified in the agreement. The termination or expiration of the GSK license agreement does not relieve either party from any obligation which accrued prior to the termination or expiration. Among other provisions, the milestone payment obligations survive termination or expiration for any reason, and the license rights granted to GSK survive expiration of the GSK license agreement. The license rights and payment obligations of GSK under the Amended GSK supply agreement survive termination or expiration, except that GSK s license rights and future royalty obligations do not survive if we terminate due to GSK s material breach unless we elect otherwise.

We understand that QS-21 is a key component included in several of GSK s proprietary adjuvant systems and a number of GSK s vaccine candidates currently under development are formulated using adjuvant systems containing QS-21. GSK has ongoing Phase 3 studies evaluating its investigational MAGE-A3 Antigen-Specific Cancer Immunotherapeutic containing QS-21 in melanoma and non-small cell lung cancer. Data from Phase 3 trials in melanoma, non-small cell lung cancer, malaria and shingles is anticipated to be reported within the next year or so.

In October 2011, *The New England Journal of Medicine* published results of a Phase 3 trial of GSK Biologicals RTS,S malaria vaccine candidate containing QS-21. Results of the study, the largest malaria vaccine efficacy and safety trial ever conducted, demonstrate that RTS,S provided young African children with significant protection against clinical and severe malaria reducing risk by 56 percent and 47 percent, respectively, for the 12-month period following vaccination. Data from a second Phase 3 trial of RTS,S is anticipated to be reported during the fourth quarter of 2012.

*Elan/JANSSEN Alzheimer s Immunotherapy.* Elan Pharmaceuticals, Inc. and/or its affiliates ( Elan ) had a commercial license for the use of QS-21 in the research and commercialization of Elan s Alzheimer s disease vaccine candidate that contains QS-21 ( Licensed Product ). Effective September 14, 2009, we entered into an Amended and Restated License Agreement ( Amended License Agreement ) with Elan, and on September 17, 2009, the Amended License Agreement was assigned to JANSSEN AI. Under the terms of the Amended License Agreement, JANSSEN AI has the right to develop, make, have made, use, sell, offer for sale, import, and have sold, the Licensed Product. In addition, pursuant to the terms of the Amended License Agreement, JANSSEN AI has the right to manufacture all of its requirements of QS-21 for use in the Licensed Product and we have no further supply obligations. Assuming all benchmarks are met under this agreement, we could receive up to $11.5 million in future milestone payments; $1.5 million has been received as of December 31, 2011. Furthermore, under the terms of the Amended License Agreement, we are entitled to receive mid single-digit royalties on net sales of the Licensed Product for a period of at least 10 years after the first commercial sale of such product, if any. Expiration or termination of the Amended License Agreement is without prejudice to any rights that accrued to the benefit of the parties prior to the date of such expiration or termination. Upon expiration of the Amended License Agreement, JANSSEN AI will have a royalty-free license. Upon early termination of the Amended License Agreement, JANSSEN AI license rights terminate and future payment obligations do not accrue.

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***Manufacturing***

Except in the case of GSK and JANSSEN AI, we have retained worldwide manufacturing rights for QS-21. We have the right to subcontract manufacturing for QS-21 and we have a supply agreement with a contract manufacturer for the production of QS-21 through September 2012. In addition, under the terms of our agreement with GSK, GSK is contractually committed to supply certain quantities of commercial grade QS-21 to us and our licensees in the future.

**Heat Shock Protein Technology**

Heat shock proteins, also known as HSPs, are also called stress proteins, as their expression is increased when cells experience various stresses like extremes of temperature (hot or cold) and oxygen deprivation. HSPs are present in all cells in all life forms from bacteria to mammals, and their structure and function are similar across these diverse life forms. Under normal conditions, HSPs play a major role in protein folding and transport of protein fragments called peptides within a cell, and are thus also known as chaperones. Antigenic peptides, those portions of a protein that stimulate immune responses when recognized by the immune cells, are also transported by these chaperones. Because HSPs interact with and bind many cellular proteins and peptides, they chaperone a broad array of antigenic peptides to facilitate their recognition by the immune system. Thus, HSPs play an integral role in capturing and presenting the antigenic fingerprint of a cell to a host s immune system.

Although HSPs are normally found inside cells, they also provide important danger signals when found outside of cells. Detection of HSPs outside of cells is indicative that cell death has occurred. This may have been caused by disease, mutation, or injury, whereby a cell s contents are spilled into body tissue. These HSPs send powerful danger signals to the immune system that initiate a cascade of events capable of generating a targeted immune response against the infection or disease-related cell death.

Combined, these functions of HSPs form the basis of our technology. The chaperoning nature of HSPs allows us to produce vaccines containing the antigenic fingerprint of a given disease. In the case of cancer, the vaccines are patient-specific, consisting of heat shock protein-peptide complexes, also known as HSPPCs, purified from a patient s tumor cells. These HSPPCs, when injected into the skin, are expected to stimulate a powerful cellular immune response potentially capable of targeting and killing the cancer cells from which these complexes were derived. Because cancer is a highly variable disease from one patient to another, due to rapid mutation of cancer cells, we believe that a patient-specific vaccination approach is required to generate a more robust and targeted immune response against the disease.

For certain diseases, such as genital herpes, we do not believe that a personalized vaccination approach is required, since the pathogen does not vary as greatly from patient to patient as do cancer cells. For example, in our HerpV product candidate for the treatment of genital herpes, we complex, or bind, several defined antigenic herpes peptides to an HSP (Hsc70) that we genetically engineer, creating an HSPPC. This HSPPC, when injected into the skin, is designed to elicit a cellular immune response to the synthetic peptides carried by the HSP.

***The Prophage Series Vaccines***

The Prophage Series vaccines describe our portfolio of patient-specific HSP-based therapeutic cancer vaccines, including the R-Series candidates in RCC, M-Series candidates in melanoma, and G-Series candidates in glioma. The first product derived from the R-Series (R-100, registered in Russia as Oncophage), represents the only approved treatment for adjuvant or non-metastatic kidney cancer patients at intermediate risk for disease recurrence.

In December 2011, we signed a license, development and manufacturing technology transfer agreement ( NewVac Agreement ) for Oncophage with NewVac LLC (a subsidiary of ChemRar Ventures LLC, NewVac ), a company focused on the development of innovative technology for cancer immunotherapy. Under the NewVac Agreement, we granted NewVac 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. The NewVac

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Agreement may be terminated by either party upon a material breach if the breach is not cured within the time specified in the agreement. The NewVac Agreement may also be terminated by us if certain milestones are not achieved and by NewVac without cause. Unless the NewVac Agreement is earlier terminated or extended, we are entitled to receive modest milestone payments in addition to payments for supply of Oncophage and/or royalties in the low double-digits on net sales of Oncophage through December 2014. Upon termination of the NewVac Agreement, all activity under the agreement immediately ceases.

Each Prophage Series vaccine candidate is made from a patient s tumor tissue. After a surgeon removes a patient s tumor, the majority of that tumor tissue is frozen and shipped to our manufacturing facility. Using a proprietary manufacturing process that takes approximately eight to 10 hours per individual patient lot, we isolate the HSPPCs from the tumor tissue. Through this isolation process, the HSPPCs are extracted, purified, and sterile-filtered from the tumor tissue, then formulated in solution and packaged in standard single-injection vials. After the performance of quality control testing, including sterility testing, we ship the frozen vaccine back to the hospital or clinic for administration. Medical professionals administer the vaccine by injecting the product into the skin.

Although we believe that our technology is applicable to all cancer types, our initial focus with the Prophage Series vaccines is on cancers that have limited or no available treatment options and in cancers that typically yield sufficient quantities of tumor tissue from the surgical procedure to allow for manufacture.

Since the first patient was enrolled in a clinical trial studying a Prophage Series vaccine in 1997, nearly 900 cancer patients have been treated with our vaccine in clinical trials. Collectively, results across all trials provided evidence of manufacturing and logistical feasibility as well as an initial demonstration of safety and signals of efficacy, which included patients who had complete disappearance (a complete response), substantial shrinkage (partial response), minor shrinkage (minor response), or no change in the size (disease stabilization) of tumor lesions. Median overall survival results exceeded historical controls that were relevant at the time when the studies were performed. Additionally, tumor-specific T-cell responses were noted in studies where they were measured, namely melanoma and colorectal cancer.

Because our Prophage Series vaccines are derived from the patient s own tumor, they are unlike the majority of approved therapies and as such, they are experiencing a long development process and incurring high development costs, either of which could delay or prevent our commercialization efforts. For additional information regarding regulatory risks and uncertainties, please read the risks identified in Part 1-Item 1A. Risk Factors of this Annual Report on Form 10-K.

***Phase 3 Renal Cell Carcinoma Program***

Renal cell carcinoma is the most common type of kidney cancer. The American Cancer Society estimates that there will be 64,770 new cases of kidney cancer and 13,570 people will die from the disease in the United States in 2012. The Kidney Cancer Research Bureau, a Russian non-profit, non-government research organization, estimated that in 2008, approximately 16,000 Russians would be diagnosed with kidney cancer and approximately 50% of those diagnosed would die of the disease.

We initiated a Phase 3, multicenter, international trial for non-metastatic RCC into which the first patient was randomized in February 2001. As announced on March 24, 2006, the trial did not reach statistical significance in its primary endpoint of recurrence-free survival in the total patient population, though a positive trend was observed. During the protocol design process in 1999 and 2000, key opinion leaders were consulted, and the non-metastatic RCC patient population designated for enrollment in the trial was thought to be a relatively uniform group. In 2006, the Eastern Cooperative Oncology Group ( ECOG ) initiated a trial in adjuvant RCC with sorafenib and sunitinib that stratified their patient population into intermediate-risk, high-risk, and very high-risk recurrence categories. Using these ECOG defined criteria, analysis of the intermediate risk patients (362 of the 604 eligible patients in the trial) in the trial showed a statistically significant difference in recurrence-free survival in favor of the Oncophage arm. In part because the intermediate-risk category was not

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prospectively delineated prior to the trial s initiation, the Food & Drug Administration ( FDA ) has indicated that, by itself, part I of our Phase 3 clinical trial in renal cell carcinoma is not sufficient to support a biologics license application ( BLA ) filing.

In April 2008, the Russian Ministry of Public Health issued a registration certificate for the use of Oncophage for the treatment of kidney cancer patients at intermediate risk for disease recurrence. Because, among other things, we have limited resources and minimal sales and marketing experience, commercialization of Oncophage has been slow, and only modest sales of Oncophage in Russia have occurred. The Russian registration was our first product approval from a regulatory authority, and the first approval of a patient-specific therapeutic cancer vaccine in a major market. In December 2011, as noted above, we out-licensed this program to NewVac.

In 2008, we announced the submission of a marketing authorization application ( MAA ) to the European Medicines Agency ( EMA ) requesting conditional authorization of Oncophage in earlier-stage, localized kidney cancer. On November 20, 2009, we announced that the Committee for Medicinal Products for Human Use ( CHMP ) of the EMA formally adopted a negative opinion on our MAA. Subsequently we withdrew our application and we are no longer actively pursuing activities in the European market. Although we are no longer in active discussions with a potential partner for the European market, we continue to actively seek partnership discussions for multiple products generated from our portfolio of Prophage Series vaccines.

***Glioma***

Glioma is a cancer affecting the central nervous system that begins in glial cells (connective tissue cells that surround and support nerve cells). Malignant glioma is currently a fatal disease. The American Cancer Society estimates that 22,910 new cases of the brain and other nervous system cancers will be diagnosed during 2012 in the U.S., and that about 13,700 people will die from these tumors.

Phase 2 trials testing the Prophage Series candidates G-100 and G-200 are underway in both newly diagnosed and recurrent glioma, respectively, where promising data has been generated to date. A Phase 2 clinical trial with Prophage Series vaccine G-200 in recurrent, high-grade glioma is currently ongoing. This study is being led by the Brain Tumor Research Center at the University of California, San Francisco ( UCSF ), with grants from the American Brain Tumor Association and the National Cancer Institute Special Programs of Research Excellence. The study, which is designed to enroll approximately 50 patients, has expanded to include New York-Presbyterian Hospital/Columbia University Medical Center and University Hospitals/Case Western Reserve.

On June 6, 2011, results from the ongoing Phase 2 clinical trial were presented at the 47$^{th}$ Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, Illinois. Results from this trial showed that 93 percent of the patients were alive at $\geq$ 26 weeks after surgery and a median overall survival of 11 months (47.6 weeks). Results from pre-defined exploratory analyses of disease progression showed a median progression free survival (PFS) of approximately 5 months (20 weeks). Importantly, measures of immune response post vaccination with Prophage Series G-200 demonstrated a significant tumor-specific CD8+ T-cell response as well as innate immune responses as marked by a significant increase in levels of circulating NK cells.

UCSF also initiated an additional Phase 2 clinical trial in newly diagnosed glioma testing Prophage Series vaccine G-100 in combination with Temodar® (temozolomide). This trial is currently enrolling, with a target of 50 patients.

***Manufacturing***

Commercial and clinical supplies of Oncophage and other vaccine candidates deriving from the Prophage Series are manufactured in our Lexington, Massachusetts facility. We estimate that this facility could support the production of up to 4,000 batches per year. On average, it takes eight to 10 hours of direct processing time to manufacture a patient batch of vaccine.

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After manufacturing, Prophage Series vaccines are tested and released by our quality systems staff. The quality control organization performs a series of release assays designed to ensure that the product meets all applicable specifications. Our quality assurance staff also reviews manufacturing and quality control records prior to batch release in an effort to assure conformance with current Good Manufacturing Practices, also known as cGMP, as mandated by the FDA and foreign regulatory agencies.

Our manufacturing staff is rigorously trained and routinely evaluated for conformance to manufacturing procedures and quality standards. This oversight is intended to ensure compliance with FDA and foreign regulations and to provide consistent vaccine output. Our quality control and quality assurance staff is similarly trained and evaluated as part of our effort to ensure consistency in the testing and release of the product, as well as consistency in materials, equipment, and facilities.

***HerpV***

HerpV is an investigational therapeutic vaccine candidate directed at the virus that causes genital herpes (herpes simplex virus-2, or HSV-2) and is the first potential recombinant (off-the-shelf) application of our HSP technology. HerpV includes our proprietary QS-21 Stimulon adjuvant. HerpV is a multivalent vaccine containing multiple synthetic HSV-2 peptides, which means that it may be applicable to a broader patient population and may have potential in managing outbreaks and disease transmission.

According to the Centers for Disease Control, genital herpes affects more than 60 million Americans or 1 in 6 people between the ages 14 and 49 with an additional 1.5 million new cases contracted each year. This disease often results in recurrent painful sores in the genital area. Current therapies involve taking a daily medication that only partly suppresses the virus.

Based on the results of completed toxicology studies and other preclinical activities, we submitted to the FDA an investigational new drug application ( IND ) for HerpV during the second quarter of 2005. In October 2005, we initiated a multicenter Phase 1 clinical trial of HerpV in genital herpes. In this four-arm, phase 1 study, 35 HSV-2 seropositive patients received HerpV with QS-21, HerpV alone, QS-21 alone, or placebo. The vaccine was well tolerated, with injection site pain as the most common reported adverse event. All patients who were evaluable for immune response and received HerpV with QS-21 showed a statistically significant CD4+ T cell response (100%; 7/7) to HSV-2 antigens as detected by IFNy Elispot, and the majority of those patients demonstrated a CD8+ T cell response (75%; 6/8). This study is the first to demonstrate that HSPs complexed to viral antigens induce an antigen-specific T cell response in humans. The results from this study were published in the peer-reviewed journal *Vaccine* in September 2011.

We believe this is a first of its kind finding in genital herpes treatment. We consider HerpV to be part of a platform technology, since with the integration of heat shock proteins with antigenic peptides, we could potentially create therapeutic vaccines for many infectious diseases. We plan to advance HerpV into a Phase 2 study in 2012 that will measure the effect of vaccination on viral shedding in individuals infected with HSV-2. Experts in HSV-2 clinical research believe that a reduction in viral shedding could translate into clinical benefit.

**Intellectual Property Portfolio**

We seek to protect our technologies through a combination of patents, trade secrets and know-how and currently have exclusive rights, through outright ownership or through exclusive licenses, to 74 issued United States patents and 113 issued foreign patents. We also have exclusive rights to 6 pending United States patent applications and 25 pending foreign patent applications. While we have patent coverage in Russia for Oncophage, we may not have rights in other territories where we may pursue regulatory approval for Prophage Series vaccine candidates.

Our issued patents include those that cover our core technologies including HSPs for the treatment of cancers and infectious disease, and saponin adjuvants.

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The issued patents that cover the Prophage Series vaccines expire at various dates between 2015 and 2024. The issued patents to HerpV expire at various dates between 2014 and 2017. Our patent to purified QS-21 expired in most territories in 2008. Additional protection for QS-21 in combination with other agents is provided by our other issued patents which expire between 2016 and 2019.

Various patents and patent applications have been exclusively licensed to us by the following entities:

***Mount Sinai School of Medicine***

In November 1994, we entered into a patent license agreement with the Mount Sinai School of Medicine (the Mount Sinai Agreement ). Through the Mount Sinai Agreement, we obtained an exclusive, worldwide license to patent rights relating to the heat shock protein technology that resulted from the research and development performed by Dr. Pramod Srivastava, our founding scientist and a former member of our Board of Directors. We agreed to pay Mount Sinai a royalty on the net sales of products covered by the licensed patent rights and also provided Mount Sinai with a 0.45% equity interest in the Company (approximately 10,300 shares) valued at approximately $90,000 at the time of issuance. The term of the Mount Sinai Agreement ends when the last of the licensed patents expires (2018) or becomes no longer valid. If we fail to pay royalties that are due under the agreement, Mount Sinai may issue written notice to us. If we continue to fail to pay royalties after 60 days from receipt of the written notice, Mount Sinai can terminate the agreement. The Mount Sinai Agreement requires us to use due diligence to make the products covered by the licensed patent rights commercially available, including a requirement for us to use best efforts to reach a number of developmental milestones, which have been achieved. If we fail to comply with the due diligence provisions of the agreement, Mount Sinai could take actions to convert our exclusive license to a non-exclusive license after six months written notice. The Mount Sinai Agreement does not contain any milestone payment provisions.

***Fordham University***

During 1995, Dr. Srivastava moved his research to Fordham University ( Fordham ). We entered into a sponsored research and technology license agreement with Fordham in March 1995 (the Fordham Agreement ) relating to the continued development of the heat shock protein technology and agreed to make payments to Fordham to sponsor Dr. Srivastava s research. Through the Fordham Agreement, we obtained an exclusive, perpetual, worldwide license to all of the intellectual property, including all the patent rights, which resulted from the research and development performed by Dr. Srivastava at Fordham. We also agreed to pay Fordham a royalty on the net sales of products covered by the Fordham Agreement through the last expiration date on the patents under the agreement (2018) or when the patents become no longer valid. The agreement does not contain any milestone payment provisions or any diligence provisions. Dr. Srivastava moved his research to the University of Connecticut Health Center ( UConn ) during 1997 and, accordingly, the parts of the agreement related to payments for sponsored research at Fordham terminated in mid-1997. During the term of this agreement, we paid Fordham approximately $2.4 million.

***University of Connecticut***

In May 2001, we entered into a license agreement with UConn which was amended in March 2003 and June 2009. Through the license agreement, we obtained an exclusive worldwide license to patent rights resulting from inventions discovered under a research agreement that was effective from February 1998 until December 2006. The term of the license agreement ends when the last of the licensed patents expires (2022) or becomes no longer valid. UConn may terminate the agreement: (1) if, after 30 days written notice for breach, we continue to fail to make any payments due under the license agreement, or (2) we cease to carry on our business related to the patent rights or if we initiate or conduct actions in order to declare bankruptcy. We may terminate the agreement upon 90 days written notice. The license agreement contains aggregate milestone payments of approximately $1.2 million for each product we develop covered by the licensed patent rights. These milestone payments are contingent upon regulatory filings, regulatory approvals, and commercial sales of products. We have also agreed to pay UConn a royalty on the net sales of products covered by the license agreement as well as annual license maintenance fees beginning in May 2006. Royalties otherwise due on the net sales of products covered by the

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license agreement may be credited against the annual license maintenance fee obligations. Under the March 2003 amendment, we agreed to pay UConn an upfront payment and to make future payments for each patent or patent application with respect to which we exercised our option under the research agreement. As of December 31, 2011, we have paid approximately $340,000 to UConn under the license agreement. The license agreement gives us complete discretion over the commercialization of products covered by the licensed patent rights but also requires us to use commercially reasonable diligent efforts to introduce commercial products within and outside the United States. If we fail to meet these diligence requirements, UConn may be able to terminate the license agreement.

**Regulatory Compliance**

Governmental authorities in the United States and other countries extensively regulate the preclinical and clinical testing, manufacturing, labeling, storage, record keeping, advertising, promotion, export, marketing and distribution, among other things, of our investigational product candidates. In the United States, the FDA under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act and other federal statutes and regulations, subject pharmaceutical products to rigorous review.

In order to obtain approval of a new product from the FDA, we must, among other requirements, submit proof of safety and efficacy as well as detailed information on the manufacture and composition of the product. In most cases, this proof entails extensive preclinical, clinical, and laboratory tests. Before approving a new drug or marketing application, the FDA may also conduct pre-licensing inspections of the company, its contract research organizations and/or its clinical trial sites to ensure that clinical, safety, quality control, and other regulated activities are compliant with Good Clinical Practices, or GCP, or Good Laboratory Practices, or GLP, for specific non-clinical toxicology studies. The FDA may also require confirmatory trials, post-marketing testing, and extra surveillance to monitor the effects of approved products, or place conditions on any approvals that could restrict the commercial applications of these products. Once approved, the labeling, advertising, promotion, marketing, and distribution of a drug or biologic product must be in compliance with FDA regulatory requirements.

In Phase 1 clinical trials, the sponsor tests the product in a small number of patients or healthy volunteers, primarily for safety at one or more doses. Phase 1 trials in cancer are often conducted with patients who have end-stage or metastatic cancer. In Phase 2, in addition to safety, the sponsor evaluates the efficacy of the product in a patient population somewhat larger than Phase 1 trials. Phase 3 trials typically involve additional testing for safety and clinical efficacy in an expanded population at geographically dispersed test sites. The FDA may order the temporary or permanent discontinuation of a clinical trial at any time.

The sponsor must submit to the FDA the results of preclinical and clinical testing, together with, among other things, detailed information on the manufacture and composition of the product, in the form of a new drug application or, in the case of biologics, like the Prophage Series vaccines, a BLA. In a process that can take a year or more, the FDA reviews this application and, when and if it decides that adequate data is available to show that the new compound is both safe and effective for a particular indication and that other applicable requirements have been met, approves the drug or biologic for marketing.

Whether or not we have obtained FDA approval, we must generally obtain approval of a product by comparable regulatory authorities of international jurisdictions prior to the commencement of marketing the product in those jurisdictions. We are also subject to cGMP, GCP, and GLP compliance obligations, and are subject to inspection by international regulatory authorities. International requirements may in some circumstances be more rigorous than U.S. requirements and may require additional investment in manufacturing process development, non-clinical studies, clinical studies, and record keeping that are not required for U.S. regulatory compliance or approval. The time required to obtain this approval may be longer or shorter than that required for FDA approval and can also require significant resources in time, money, and labor.

Under the laws of the United States, the countries of the European Union, and other nations, we and the institutions where we sponsor research are subject to obligations to ensure the protection of personal information of human subjects participating in our clinical trials. We have instituted procedures that we believe will enable us

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to comply with these requirements and the contractual requirements of our data sources. The laws and regulations in this area are evolving, and further regulation, if adopted, could affect the timing and the cost of future clinical development activities.

We are also subject to regulation under the Occupational Safety and Health Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, and other current and potential future federal, state, or local regulations. Our research and development activities involve the controlled use of hazardous materials, chemicals, biological materials, various radioactive compounds, and for some experiments we use recombinant DNA. We believe that our procedures comply with the standards prescribed by local, state, and federal regulations; however, the risk of injury or accidental contamination cannot be completely eliminated. We conduct our activities in compliance with the National Institutes of Health Guidelines for Recombinant DNA Research.

**Competition**

Competition in the pharmaceutical and biotechnology industries is intense. Many pharmaceutical or biotechnology companies have products on the market and are actively engaged in the research and development of products for the treatment of cancer and infectious diseases. In addition, many competitors focus on immunotherapy as a treatment for cancer and infectious diseases. In particular, some of these companies are developing cancer vaccines produced from a patient s own cells or tissue. Others are focusing on developing heat shock protein products. Prior to regulatory approval, we 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. In addition, we compete for funding, access to licenses, personnel, and third-party collaborations. Many competitors have substantially greater financial, manufacturing, marketing, sales, distribution, and technical resources, and more experience in research and development, clinical trials, and regulatory matters, than we do. Competing companies developing or acquiring rights to more efficacious therapeutic products for the same diseases we are targeting, or which offer significantly lower costs of treatment, could render our products noncompetitive or obsolete. See Part I-Item 1A. Risk Factors Our competitors in the biotechnology and pharmaceutical industries may have superior products, manufacturing capability, selling and marketing expertise and/or financial and other resources.

Academic institutions, governmental agencies, and other public and private research institutions conduct significant amounts of research in biotechnology, medicinal chemistry, and pharmacology. These entities have become increasingly active in seeking patent protection and licensing revenues for their research results. They also compete with us in recruiting and retaining skilled scientific talent.

We are aware of certain programs and products under development by other companies that may compete with our programs and products. Several of these companies have products that utilize similar technologies and/or patient-specific medicine techniques. Genentech markets Avastin and Eisai markets Gliadel, both for treatment of recurrent glioma. In addition, TVAX Biomedical is developing an immunotherapy candidate (TVI-Brain-1) 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) and Celldex (CDX-110). One or more of these companies may also develop product candidates for recurrent glioma.

Valtrex (GSK) and Famvir (Novartis) are small molecule drugs marketed for treatment of genital herpes. Other companies are engaged in research for vaccines for treatment of genital herpes. 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 identical to QS-21 that are being used in clinical trials. Several other vaccine adjuvants are in development and could compete with QS-21 for inclusion in vaccines in development. These adjuvants include, but are not limited to, oligonucleotides, under development by Pfizer, Idera, Juvaris, and Dynavax, MF59 under development by Novartis, IC31, under development by Intercell, and

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MPL, under development by GSK. Companies such as Adjuvance Technologies, Inc. and CSL Limited, as well as academic institutions, are developing saponin adjuvants, including derivatives and synthetic formulations. It is possible that these compounds could be substituted for the Company s QS-21.

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.

**Employees**

As of February 24, 2012, we had approximately 54 employees, of whom 8 were Ph.D.s and 2 were MDs. None of our employees are subject to a collective bargaining agreement. We believe that we have good relations with our employees.

**Corporate History**

Antigenics L.L.C. was formed as a Delaware limited liability company in 1994 and was converted to Antigenics Inc., a Delaware corporation, in February 2000 in conjunction with our initial public offering of common stock. As of January 6, 2011, we changed our name from Antigenics Inc. to Agenus Inc. to more accurately reflect our existing product pipeline, which has expanded over the years beyond antigen-based vaccines, as well as to highlight our business strategy as we seek partnering opportunities to grow and diversify our business.

**Availability of Periodic SEC Reports**

Our Internet website address is *www.agenusbio.com*. We make available free of charge through our website our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 ( Securities Exchange Act ) as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the Securities and Exchange Commission (the SEC ). The contents of our website are not part of, or incorporated into, this document.

**Item 1A.** ***Risk Factors***

Our future operating results could differ materially from the results described in this Annual Report on Form 10-K due to the risks and uncertainties described below. We cannot assure investors that our assumptions and expectations will prove to be correct. Important factors could cause our actual results to differ materially from those indicated or implied by forward-looking statements. See Note Regarding Forward-Looking Statements in this Annual Report on Form 10-K. Factors that could cause or contribute to such differences include those factors discussed below.

**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.***

From our inception through December 31, 2011, we have incurred net losses totaling $607.7 million. Our net losses for the years ended December 31, 2011, 2010, and 2009, were $23.3 million, $21.9 million, and $30.3 million, respectively. We expect to incur significant losses over the next several years as we continue research and clinical development of our technologies, apply for regulatory approvals, and pursue partnering opportunities, 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 QS-21, our Prophage Series vaccines and our other product candidates. 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.

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On December 31, 2011, we had $10.7 million in cash and cash equivalents. We believe that, based on our current plans and activities, our working capital resources at December 31, 2011 and the net proceeds raised from equity sales and license agreements since year-end, along with the estimated proceeds from our license, supply, and collaborative agreements, will be sufficient to satisfy our liquidity requirements through 2013 based on our estimated annual use of cash of $13-16 million during 2012. 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 year ended December 31, 2011, our average monthly cash used in operating activities was $1.4 million. We do not anticipate significant capital expenditures during 2012.

We have financed our operations primarily through the sale of equity and convertible notes. 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, we will be required to delay, reduce, or eliminate some or all of our development, commercialization and clinical trial programs. 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. We may also be unable to continue our operations, or we may become insolvent.

The weakness of the United States economy and the global economy 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 further deterioration in the credit markets and related financial crisis on our collaborative partners could limit potential revenue from our product candidates.

***We have significant debt, and we may not be able to make interest or principal payments when due.***

As of December 31, 2011, we had debt outstanding of $37.9 million in principal, including $37.5 million in principal of our 8% senior secured convertible notes due August 2014 (the 2006 Notes ) and $100,000 in principal of our 5.25% convertible senior notes due February 2025 (the 2005 Notes ). The 2005 Notes are currently subject to redemption at our option or at the options of the holders on each of February 1, 2015 and February 1, 2020.

Our ability to satisfy our obligations 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.

To date, we have had negative cash flows from operations. For the years ended December 31, 2011, 2010, and 2009, net cash used in operating activities was $16.2 million, $14.8 million, and $24.2 million, respectively.

***Our 2006 Notes contain restrictive covenants and are convertible into equity interests in one of our subsidiaries that holds important rights to certain of our QS-21 Stimulon® adjuvant and HerpV technology.***

Our 2006 Notes are secured by the equity of our wholly-owned subsidiary that holds the QS-21 and HerpV technologies. At the option of the holders, our 2006 Notes can be converted in whole or in part into an equity interest in this subsidiary, subject to our ability to preempt the conversion by redeeming the 2006 Notes to be so

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converted at a price equal to the conversion amount of such notes plus an amount that, when taken together with any cash interest payments previously made with respect to such 2006 Notes, would generate a 30% annual internal rate of return to the holders. If converted into an equity interest of this subsidiary, the ownership interest in the subsidiary will be determined by multiplying (x) the quotient of the conversion amount divided by $25.0 million, by (y) 30%. In addition, our 2006 Notes grant holders a right of first refusal in any future equity issuance in this subsidiary so that holders of our 2006 Notes may purchase up to 50% of any newly issued equity in this subsidiary. In addition, our 2006 Notes contain a number of restrictions and covenants, including, but not limited to, restrictions and covenants that limit our ability, and the ability of our subsidiary mentioned above, to:

- incur certain additional indebtedness;
- make certain investments;
- enter into certain affiliated party transactions;
- create certain liens;