AGENUS INC
Form 10-K
March 16, 2011
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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, 2010

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). ¨

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, 2010 was: $67.8 million. There were 112,653,700 shares of the registrant s Common Stock outstanding as of March 1, 2011.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement for the registrant s 2011 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, 2010, 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. One 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 future research and development, our product development efforts, our ability to commercialize our product candidates, our sales and marketing activities in Russia, our prospects for initiating partnerships or collaborations, the timing of the introduction of our 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. The Company has included important factors in the cautionary statements included in this Annual Report, particularly under Item 1A. Risk Factors, that the Company believes could cause actual results to differ materially from any forward-looking statement.

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

We have included more detailed descriptions of these risks and uncertainties and other risks and uncertainties applicable to our business in 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.

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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, primarily based on immunological approaches. 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. In conjunction with this name change, our autologous cancer immunotherapies have been named the Prophage Series of cancer vaccines (vitespen; HSPPC-96). The name Oncophage® vaccine will be retained in the adjuvant renal cell carcinoma indication as part of the Prophage Series. AG-707 was renamed HerpV.

Some of our key assets are highlighted below:

The Prophage Series of cancer vaccines: The Prophage Series of cancer vaccines is based on our core heat shock protein technology. We believe that the collective results from our clinical trials to date indicate a favorable safety profile and signals of efficacy in multiple cancer types. In a registry following patients from a large randomized Phase 3 trial in non-metastatic renal cell carcinoma (RCC; kidney cancer), patients at intermediate risk of recurrence who were in the treatment arm 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). This product is approved for sale in this indication in Russia. Phase 2 trials are underway testing the Prophage Series vaccines G-100 and G-200 in newly diagnosed and recurrent glioma, respectively. 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. Additional trials are under evaluation in metastatic RCC and metastatic melanoma in combination with potentially synergistic therapies, as well as in pediatric neurological tumors.

QS-21 Stimulon® adjuvant (QS-21): QS-21 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. There are 14 vaccines containing QS-21 in clinical development, including four in Phase 3 testing for malaria, melanoma, non-small cell lung cancer and shingles. The first products containing QS-21 are expected to be launched in the 2013-2014 timeframe, and we are 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 and are generally reimbursed for any related expenses by our licensees.

HerpV: HerpV is a therapeutic vaccine for the treatment of genital herpes, which is based on our HSP technology. 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 are currently seeking partners to advance HerpV and the platform technology into further development.

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In addition to our internal development efforts, we are actively pursuing multiple partnering opportunities. We are seeking regional and/or global partners for select products in our portfolio, including Oncophage, the Prophage G-Series vaccines, G-100 and G-200, and HerpV. We are also exploring a variety of in-licensing opportunities that would be complementary to our existing business while expanding our product pipeline. 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, 2010, 2009, and 2008, were $12.9 million, $16.9 million, and $20.7 million, respectively.

On March 3, 2011, we were notified by the Listing Qualifications Staff of Nasdaq indicating that we are not in compliance with the 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. In accordance with Nasdaq Marketplace Rule 5810(c)(3)(A), we have been provided 180 calendar days, or until August 30, 2011, to regain compliance with the Bid Price Requirement.

Our Products and Technologies Under Development

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 of Cancer Vaccines

The Prophage Series of cancer vaccines describes our portfolio of patient-specific HSP-based therapeutic cancer vaccines, including the R-Series candidates in RCC, M-Series candidates in melanoma, G-Series

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candidates in glioma, and NP-Series candidate in pediatric neurological tumors. 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 2008, we submitted a marketing authorization application (MAA) to the European Medicines Agency (EMA) requesting approval for Oncophage in earlier-stage, localized kidney cancer under the conditional authorization provision. After its review, the Committee for Medicinal Products for Human Use (CHMP) of the EMA adopted a negative opinion on our application and subsequently we withdrew our application. In a registry following patients from our large randomized Phase 3 trial in non-metastatic RCC, patients at intermediate risk of recurrence who were in the treatment arm 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). 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. Additional trials are planned in metastatic RCC (R-200) and metastatic melanoma (M-200) in combination with potentially synergistic therapies, as well as in pediatric neurological tumors (NP-150).

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 our first patient was enrolled in a clinical trial studying a Prophage Series vaccine in 1997, we have treated more than 850 cancer patients in our clinical trials. Because our vaccines are derived from the patient s own tumor, they are unlike the majority of approved therapies and as such, they may experience a long regulatory review process and 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 under Risk Factors.

We believe that the collective results from our clinical trials thus far show that the vaccine candidates that have been clinically evaluated have a favorable safety profile. We also believe that available results from clinical trials suggest that treatment with the Prophage Series vaccines can generate immunological and anti-tumor responses.

Phase 3 Renal Cell Carcinoma Program

Renal cell carcinoma is the most common type of kidney cancer. The American Cancer Society estimated that there would be 58,240 new cases of kidney cancer and 13,040 people would die from the disease in the United States in 2010. 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,

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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 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.

We opened a subsequent protocol that continued to follow patients from this trial in the format of a registry in order to collect overall survival information, as well as investigator reports of disease recurrence. The registry, which is expected to provide additional data on the effectiveness of Oncophage, followed patients until March 2010, an additional three years from closure of the initial trial, providing more than five years of data collection following the enrollment of the last patient in the trial. Final analysis of this data is in process. At the 2009 American Society of Clinical Oncology (ASCO) annual meeting, we announced results of an interim analysis from the ongoing global patient survival registry, which showed that patients with kidney cancer at intermediate risk of disease recurrence demonstrated an approximately 46 percent lower risk of death when treated with Oncophage cancer vaccine after surgery compared with no treatment (n = 362; $P < 0.05$; hazard ratio = 0.54).

In addition to the patient registry, patient enrollment has commenced into a small study in non-metastatic RCC to assess immune response in the intermediate-risk patient population. The results of this study, continued data collection through the survival registry, and ongoing analysis are uncertain, and may not positively affect the acceptability of the overall results of the trial and, even if clinically meaningful, may not meet the requirements of the FDA or other regulatory authorities for submission and approval of a marketing application or similar applications for product approval outside the United States.

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 during the year ended December 31, 2010. 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. Since this approval we have been focusing our efforts in Russia on securing one or more distribution and/or partnering arrangements and related commercialization activities. The amount of any future revenue generated from the sale of Oncophage in Russia will depend on our ability to successfully execute on these efforts and identify and obtain adequate reimbursement, as well as decisions of physicians and patients, among other factors. Furthermore, we may experience significant delays in the receipt of payment for Oncophage, or an inability to collect payments at all.

In October 2008, we announced the submission of a MAA to the EMA requesting conditional authorization of Oncophage in earlier-stage, localized kidney cancer. On November 20, 2009, we announced that the CHMP of the EMA formally adopted a negative opinion on this MAA. Subsequently we withdrew our application and have been evaluating a variety of options to potentially bring Oncophage to patients and physicians globally. 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 estimated that 22,020 new cases of the brain and other nervous system cancers would be diagnosed during 2010 in the U.S., and that about 13,140 people would die from these tumors.

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A Phase 2 clinical trial with Prophage Series 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. Phase 1 results, presented at the Society for Neuro-Oncology Annual Meeting Conference in November 2008, showed that vaccination following brain cancer surgery increased overall median survival to approximately 10.5 months, with four patients surviving beyond 12 months and one patient surviving almost 2.5 years. The study also showed that all 12 treated patients demonstrated a significant immune response after vaccination with G-200 ($P < 0.001$) and that patients with minimal residual disease at time of first vaccination (n = 7) were more likely to survive beyond nine months compared with patients with significant residual disease.

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. Interim data was presented at the Society for Neuro-Oncology meeting in October 2009, which showed a median survival of 10.1 months in the first 20 patients treated with G-200, and that to date six patients (30 percent) had survived at or beyond 12 months. This early data shows an improvement in overall survival over the previous long-standing historical median survival of 6.5 months, and is also slightly favorable to the recently reported median survival of 9.2 months with Avastin® (bevacizumab) in patients with recurrent high-grade glioma. In May 2010, data presented at the International Conference on Brain Tumor Research and Therapy suggested that vaccination with this candidate may improve overall survival in patients with recurrent high-grade glioma. An overall median survival of 44 weeks after tumor resection was observed. Approximately 70% of the evaluable patients survived beyond 36 weeks, and 41% survived up to or longer than one year. Additional data from this trial will be reported by mid-2011. UCSF also initiated an additional Phase 2 clinical trial in newly diagnosed glioma testing Prophage Series G-100 in combination with Temodar® (temozolomide). This trial is currently enrolling, with a target of 50 patients. Based on promising trends to date, this trial is being expanded to include up to 10 clinical sites.

Other Clinical Trials

Initial clinical trials of Prophage Series vaccines were aimed at assessing feasibility, safety and preliminary efficacy; select studies measured immune response. A series of small, single-arm trials were performed in various solid tumor types, including RCC, melanoma, colorectal cancer, gastric cancer, pancreatic cancer, and non-small cell lung cancer. A single Phase 1 trial was conducted in non-Hodgkin s lymphoma, and a non-registrational Phase 3 trial was conducted in metastatic melanoma.

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: melanoma and colorectal cancer. In the Phase 3 metastatic melanoma trial, earlier-stage patients who received at least 10 doses of the vaccine showed a survival benefit over patients in the control arm.

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 the facility s current capacity for these products is approximately 10,000 patient courses per year, expandable to approximately 200,000 patient courses per year, by building-out currently available space, adding second and third shifts, and automating various functions. 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.

Preclinical Activities

We continue with product characterization efforts to better define the complex structure of the Prophage Series vaccines. These efforts are made more challenging by the autologous nature of the products. In addition, we are developing methods that will assess the intensity of immunological responses following vaccination with these vaccines. We expect to continue these efforts during 2011. In addition, we are currently planning to study the Prophage Series vaccine candidates in combination with potentially synergistic therapies in later-stage cancers.

QS-21

QS-21 Stimulon® adjuvant 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 Alzheimer Immunotherapy. There are 14 vaccines containing QS-21 in clinical development, including four in Phase 3 testing for malaria, melanoma, non-small cell lung cancer and shingles. The first products containing QS-21 are expected to be launched in the 2013-2014 timeframe, and we are entitled to royalties for at least 10 years post-launch. 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 and is generally reimbursed for any related expenses by its licensees.

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, a natural compound 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, nearly 14,000 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 Alzheimer Immunotherapy. 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. There are 14 vaccines currently in clinical development that contain 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. To date, we have received $10.5 million of a potential $15.3 million in upfront and milestone payments related to these agreements. We are entitled to receive low single-digit royalties on net sales for a period of at least 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 that a number of GSK s vaccine candidates currently under development are formulated using adjuvant systems containing QS-21. GSK has initiated Phase 3 studies evaluating its investigational MAGE-A3 Antigen-Specific Cancer Immunotherapeutic containing QS-21 in non-small cell lung cancer and melanoma. GSK has also initiated Phase 3 clinical trials in malaria and shingles.

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 Alzheimer Immunotherapy, a subsidiary of Johnson & Johnson. Under the terms of the Amended License Agreement, JANSSEN Alzheimer Immunotherapy has the right to develop, make, have made, use, sell, offer for sale, import, and have sold, the Licensed Product. In addition, JANSSEN Alzheimer Immunotherapy 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, 2010. Furthermore, under the terms of the Amended License Agreement, we are entitled to receive middle 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 Alzheimer Immunotherapy will have a royalty-free license. Upon early termination of the Amended License Agreement, JANSSEN Alzheimer Immunotherapy s license rights terminate and future payment obligations do not accrue.

Manufacturing

Except in the case of GSK and JANSSEN Alzheimer Immunotherapy, 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.

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 off-the-shelf application of our HSP technology.

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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.

A 2005-2008 study of the Centers for Disease Control and Prevention estimates 16.2% of people 14 to 49 years of age in the U.S. have HSV-2 infection. The World Health Organization estimated in 2003 that approximately 23.6 million people aged 15 to 49 worldwide are infected each year with HSV-2. Genital herpes is currently treated with palliative topical drugs or antiviral agents that reduce further replication of the virus during the period of treatment.

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 (63%; 5/8). This study is the first to demonstrate that HSPs complexed to viral antigens induce an antigen-specific T cell response in humans.

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 hope to advance HerpV and the platform technology in development through a partnership, and we are actively pursuing licensing discussions.

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 73 issued United States patents and 117 issued foreign patents. We also have exclusive rights to 4 pending United States patent applications and 29 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.

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 62,000 shares)

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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 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, 2010, 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

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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 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.

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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.

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, such as Dendreon and Accentia, as well as Immuncell-LC, ICT-107, DC-Vax and CDX-110, being developed by Innocell Corp, ImmunoCellular Therapeutics, Northwest Biotherapeutics and Celldex, respectively, for treatment of patients with newly diagnosed glioma.

We are aware of at least one saponin adjuvant which claims to be identical to QS-21. OPT-821 was developed by Optimer Pharmaceuticals and is being used in ongoing cancer vaccine 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 MPL, under development by GSK. In addition, at least one company, CSL Limited, as well as academic institutions, are developing saponin adjuvants, including derivatives and synthetic formulations.

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 25, 2011, we had approximately 56 employees, of whom 7 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.

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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 on page 2 of 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, 2010, we have incurred net losses totaling $584.4 million. Our net losses for the years ended December 31, 2010, 2009, and 2008, were $21.9 million, $30.3 million, and $30.8 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 commercialization of Oncophage and our various 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.

On December 31, 2010, we had $19.8 million in cash and cash equivalents. We believe that, based on our current plans and activities, our working capital resources at December 31, 2010, combined with anticipated revenues, and the estimated proceeds from our license, supply, and collaborative agreements, will be sufficient to satisfy our liquidity requirements through 2011. We expect to attempt to raise additional funds in advance of depleting our current funds. For the year ended December 31, 2010, our average monthly cash used in operating activities was $1.2 million. We do not anticipate significant capital expenditures during 2011.

We are required to maintain effective registration statements in connection with certain private placement agreements. If we are unable to keep the registration statements continuously effective in accordance with the terms of the private placement agreements, or do not maintain our listing on Nasdaq or any electronic bulletin board, we are subject to liquidated damages penalties of up to a maximum of 10% of the aggregate purchase price paid by the original investors, or up to $3.8 million.

Since our inception, we have financed our operations primarily through the sale of equity and convertible notes, interest income earned on cash, cash equivalents, and short-term investment balances, and debt provided through secured lines of credit. 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. During February 2010, we entered into an At the Market Sales Agreement with McNicoll, Lewis & Vlak LLC and Wm Smith & Co (the Sales Agents) under which we may sell an aggregate of up to 20 million shares of our common stock from time to time through the Sales Agents. To date we have sold approximately 7.0 million shares of our common stock under this agreement for net proceeds, after expenses, of $8.8 million.

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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.

At the option of the holders, our 8% senior secured convertible notes due August 2014 (the 2006 Notes) can be converted into an interest in one of our wholly-owned subsidiaries that holds the rights or patents to QS-21 and HerpV. If converted into an interest of this subsidiary, the ownership interest in the subsidiary will be determined by multiplying the quotient of the conversion amount divided by $25.0 million, by 30%. If the holders elect not to convert into the subsidiary, then at the maturity of the 2006 Notes, we may elect to repay the then outstanding balance, $34.7 million at December 31, 2010, in cash or in common stock, subject to certain limitations. In no event will any of the note holders be obligated to accept equity that would result in them owning in excess of 9.99% of our outstanding common stock at any given time in connection with any conversion, redemption, or repayment of these notes. The 2006 Notes are secured by the equity of the subsidiary that holds the rights or patents to QS-21 and HerpV.

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, 2010, 2009, and 2008, net cash used in operating activities was $14.8 million, $24.2 million, and $28.9 million, respectively.

Several factors could prevent the successful commercialization of Oncophage in Russia. In addition, we do not expect to generate significant revenue from sales of Oncophage in Russia in the near term.

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 and, in September 2008, the FDA granted the necessary permission to allow for the export of Oncophage from the United States to Russia. The Russian registration was our first product approval from a regulatory authority.

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Since approval, modest sales have occurred in Russia. Complexities unique to the logistics of this product may delay shipments and limit our ability to move commercial product in an efficient manner without incident. We currently do not have a business presence outside of the United States and rely on third parties to conduct our Oncophage operations in Russia. The reimbursement system in Russia is changing rapidly and has experienced serious funding and administrative problems in its national and regional reimbursement programs. If we are unable to obtain local distribution arrangements including favorable pricing and payment terms, and/or develop appropriate logistical processes for distribution of Oncophage, our commercialization efforts would be adversely affected.

To date we have not been able to secure government reimbursement and there appears to be a limited private-pay market in Russia. If we are unsuccessful in obtaining substantial reimbursement for Oncophage from national or regional funds, we will have to rely on private-pay for the foreseeable future, which may limit or prevent our sales efforts because the ability and willingness of patients to pay is unclear and many patients will not be capable of paying for Oncophage by themselves. Because we have limited resources and minimal sales and marketing experience, successful commercialization of Oncophage may not materialize. Furthermore, we may experience significant delays in the receipt of payment for Oncophage, or an inability to collect payments at all.

If we fail to obtain adequate levels of reimbursement for our product candidates there may be no commercially viable market for these products, or the commercial potential of these products may be significantly limited.

Public and private insurance programs may determine that they will not cover our or our collaborative partners product candidates. In Russia, Europe, and other countries outside the United States, 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 collaborative partners 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 our launch efforts, because the ability and willingness of patients to pay for our products is unclear.

It is possible that there will be substantial delays in obtaining coverage of our product candidates, or the product candidates of our licensees or collaborative partners, if at all, and that, if coverage is obtained, there may be significant restrictions on the circumstances in which there would be reimbursement. We are unable to predict what impact any future regulation or third-party payer initiatives relating to reimbursement will have on our sales.

If we fail to comply with regulatory requirements in the countries in which we conduct our business, if these regulatory requirements change, or if we experience unanticipated regulatory problems, our commercial launch of our Prophage Series product candidates could be prevented or delayed, or our product candidates could be subjected to restrictions, or be withdrawn from the market, or some other action may be taken that may be adverse to our business.

Regulatory authorities generally approve products for particular indications. If an approval is for a limited indication, this limitation reduces the size of the potential market for that product. Product approvals, once granted, are subject to continual review and periodic inspections by regulatory authorities. Later discovery of previously unknown problems or safety issues and/or failure to comply with applicable regulatory requirements can result in, among other things, warning letters, fines, injunctions, civil penalties, recall or seizure of products, total or partial suspension of production, refusal of the government to renew marketing applications, complete withdrawal of a marketing application, and/or criminal prosecution. Such regulatory enforcement could have a direct and negative impact on the product for which approval is granted, but also could have a negative impact on the approval of any pending applications for marketing approval of new drugs or supplements to approved applications.

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In addition, our operations and marketing practices are subject to regulation and scrutiny by the United States government, as well as governments of any other countries in which we do business or conduct activities. Because we are a company operating in a highly regulated industry, regulatory authorities could take enforcement action against us in connection with our business and marketing activities for various reasons.

For example, our marketing and sales, labeling, and promotional activities in Russia are subject to local regulations. If we fail to comply with regulations prohibiting the promotion of products for non-approved indications or products for which marketing approval has not been granted, regulatory authorities could bring enforcement actions against us that could inhibit our marketing capabilities, as well as result in penalties. In addition, the United States Foreign Corrupt Practices Act prohibits U.S. companies and their representatives from offering, promising, authorizing, or making payments to foreign officials for the purpose of obtaining or retaining business abroad. Failure to comply with domestic or foreign laws, knowingly or unknowingly, could result in various adverse consequences, including possible delay in approval or refusal to approve a product, recalls, seizures, withdrawal of an approved product from the market, exclusion from government health care programs, imposition of significant fines, injunctions, and/or the imposition of civil or criminal sanctions against us and/or our officers or employees.

From time to time, new legislation is passed into law that could significantly change the statutory provisions governing the approval, manufacturing, and marketing of products regulated by the FDA and other global health authorities. Additionally, regulations and guidance are often revised or reinterpreted by health agencies in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted, or whether regulations, guidance, or interpretations will change, and what the impact of such changes, if any, may be.

We may not be able to make the Prophage Series of cancer vaccines available in countries other than Russia or in indications other than renal cell carcinoma.

The Prophage Series R-100 is currently only approved for marketing in Russia as Oncophage for the adjuvant treatment of kidney cancer patients at intermediate risk for disease recurrence. The probability and timing of submissions and/or approval in any jurisdiction or indication for this product is uncertain.

In 2008, we submitted a marketing authorization application (MAA), to the European Medicines Agency (EMA), requesting conditional authorization of Oncophage in earlier-stage, localized kidney cancer. After its review, the Committee for Medicinal Products for Human Use (CHMP) of the EMA adopted a negative opinion on our MAA and subsequently we withdrew our application. If we continue to pursue a marketing authorization application for Oncophage with the EMA, there is a high level of uncertainty regarding the probability and timing of a favorable outcome. In addition, even if we continue this pursuit, Oncophage may not achieve approval in Europe because we may not successfully address issues associated with post-hoc analysis, subgroup analysis, lack of immunological data, product characterization, or other issues that may be of concern to the EMA.

The FDA has indicated that our Phase 3 clinical trials of Prophage Series R-100 (Oncophage) and M-200 cannot, by themselves, support biologics license application (BLA) filings in the studies indications (renal cell carcinoma and metastatic melanoma). The signals and trends observed in the Phase 3 renal cell carcinoma and melanoma trials are based on data analysis of subgroups of patients, some of which were not pre-specified. While the subgroup data might be suggestive of treatment effect, under current regulatory guidelines the results cannot be expected, alone, to support registration or approval in the United States, and our existing data may not support registration or approval in other territories outside of Russia, including in Europe. Due to our lack of resources, our ability to perform additional studies may be limited. Furthermore, studies may take years to complete and may fail to support regulatory filings for many reasons. In addition, our Prophage Series vaccines are a novel class of patient-specific (derived from the patient s own tumor) oncology therapies, and the FDA and foreign regulatory agencies, including the EMA, which is responsible for product approvals in Europe, and Health

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Canada, which is responsible for product approvals in Canada, have relatively little experience in reviewing these types of therapies. Therefore, Prophage Series product candidates may experience a long regulatory review process and high development costs, either of which could delay or prevent our commercialization efforts.

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

The Prophage Series vaccine R-100 is currently only approved for sale in Russia as Oncophage. Russia is an evolving market and regulatory, legal, and commercial structures are less predictable than in more mature markets. This unpredictability, as well as potential geopolitical instability in the Russian region, could negatively impact the regulatory and/or commercial environment there, which in turn could have an adverse effect on our business.

In addition, various other risks associated with foreign operations may impact our success. Possible risks include fluctuations in the value of foreign and domestic currencies, disruptions in the import, export, and transportation of patient tumors and our product, the product and service needs of foreign customers, difficulties in building and managing foreign relationships, the performance of our licensees or collaborators, and unexpected regulatory, economic, or political changes in foreign markets.

Our financial position, results of operations, and cash flows can be affected by fluctuations in foreign currency exchange rates, primarily for the euro and the ruble. Movement in foreign currency exchange rates could cause revenue or clinical trial costs to vary significantly in the future and may affect period-to-period comparisons of our operating results. Historically, we have not hedged our exposure to these fluctuations in exchange rates.

Our commercial and international operations experience and resources are limited and need to be developed or acquired. If we fail to do so, our revenues may be limited or nonexistent. In addition, we may be required to incur significant costs and devote significant efforts to augment our existing capabilities.

As we have limited experience with commercial and international operations, it may be difficult to accurately estimate our costs. We currently do not have employees, manufacturing, or business operations facilities outside of the United States and we will rely significantly on consultants, partners, and other third parties to conduct our sales, marketing, and distribution operations. If these third parties are unable to fulfill their obligations this could have a material adverse effect on our commercialization efforts. If in the future we elect to perform sales, marketing, and distribution functions ourselves, we will face a number of additional risks, including the need to recruit experienced marketing and sales personnel, or incur significant expenditures. In addition, we may need to compete with other companies that have more experienced and better-funded operations. Where we have licensed our products to third-party collaborators or licensees, we will be dependent on their commercial operations, sales and marketing expertise and resources, and any revenues we receive from those products will depend primarily on the sales and marketing efforts of others.

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 products and the products in development by our collaborative partners may fail because of intense competition from major pharmaceutical companies and specialized biotechnology companies engaged in the development of product candidates directed at cancer, infectious diseases and degenerative disorders. Several of these companies have products that utilize technologies similar to our Prophage Series and/or patient-specific or other vaccine based techniques, such as Dendreon and Accentia, as well as Immuncell-LC, ICT-107, DC-Vax and CDX-110, being developed by Innocell Corp, ImmunoCellular Therapeutics, Northwest Biotherapeutics and Celldex, respectively, for treatment of patients with newly diagnosed glioma.

There is no guarantee that we will be able to compete with potential future products being developed by our competitors. For example, Oncophage may compete with therapies currently in development for non-metastatic

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renal cell carcinoma, such as Wilex AG s Rencarex (WX-G250), which is in Phase 3 clinical trials. Additionally, sorafenib and sunitinib, which are approved for advanced renal cell carcinoma, are being studied in non-metastatic renal cell carcinoma, and other products that have been developed for metastatic renal cell carcinoma, such as temsirolimus, bevacizumab and pazopanib, may also be developed for non-metastatic renal cell carcinoma. As our Prophage Series vaccines are potentially developed in other indications, they will face additional competition in those indications. In addition, for our Prophage Series vaccines, and all of our product candidates, 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. We anticipate that we will face increased competition in the future as new companies enter markets we seek to address and scientific developments surrounding immunotherapy and other traditional cancer therapies continue to accelerate.

Our patent to purified QS-21 expired in most territories in 2008. Additional protection for our QS-21 proprietary adjuvant in combination with other agents is provided by our other patents. Our license and manufacturing agreements for QS-21 typically provide royalties for at least 10 years after commercial launch independent of patent expiry. However, there is no guarantee that we will be able to collect royalties in the future.

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 MPL, under development by GSK. In addition, at least one company, CSL Limited, as well as academic institutions, are developing saponin adjuvants, including derivatives and synthetic formulations.

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.

Manufacturing problems may cause product launch delays, unanticipated costs, or loss of revenue streams.

If the demand for our Prophage Series vaccines is substantially greater than we anticipate, our capacity may not be able to meet product demand. In addition, higher manufacturing loads may result in higher manufacturing failure rates as the operation becomes more complex. We currently manufacture our Prophage Series vaccines in our Lexington, Massachusetts facility and we intend to continue using this facility to satisfy all demands for product. While we believe we will be able to cover all demands in the near term, there is no guarantee that we will be able to meet all future or unanticipated increases in demand, and a failure to do so could adversely affect our business. Such demand may also limit our ability to manufacture product in support of clinical trials, and this could cause a delay or failure in our Prophage Series 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.

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We can also manufacture other clinical products in our own manufacturing facility. Our manufacturing facility has support areas that it shares with the Prophage Series manufacturing areas. As we seek to make Prophage Series vaccines available in other territories, the applicable 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 products such as HerpV in our current facility. In order to prepare additional HerpV to support future clinical trials, we would then have to manufacture or have manufactured this product in an appropriate alternative facility.

Currently, we do not manufacture QS-21 in our own manufacturing facility, and we have given two QS-21 licensees who have the most advanced QS-21 programs the right to manufacture QS-21 themselves or through third-party manufacturers. If these licensees are unable to successfully manufacture or have manufactured QS-21, the commercialization of the product candidates being developed by such licensees could be delayed or prevented, and we could lose important potential future revenue streams. We currently outsource the manufacture of QS-21 under an agreement that expires in 2012. If we are not able to renew this agreement we may have to identify an alternative manufacturing source or the investment of substantial funds would be required to develop our own manufacturing facility. We or our currently contracted suppliers may never have the ability to manufacture commercial grade QS-21.

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 our manufacturing facility or at our contract manufacturers 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 contract manufacturers 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.

Manufacturing is also subject to extensive government regulation. Regulatory authorities must approve the facilities in which human health care products are produced. 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.

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. 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

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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. As of December 31, 2010, we have spent approximately 16 years and $281.9 million on our research and development program in heat shock proteins for cancer.

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

Our existing Oncophage data may not support registration or approval in territories outside of Russia, including in the U.S. or Europe. Any additional studies may take years to complete and may fail to support regulatory filings for many reasons. In October 2008, we submitted a MAA to the EMA, requesting conditional authorization of Oncophage in earlier-stage, localized kidney cancer. After its review the CHMP of the EMA adopted a negative opinion on this MAA and subsequently we withdrew our application. We are currently evaluating our options to determine whether and how to proceed with Oncophage in renal cell carcinoma. If we continue to pursue a MAA for Oncophage with the EMA, there is a high level of uncertainty regarding the probability and timing of a favorable outcome. In addition, even if we continue this pursuit, Oncophage may not achieve approval in Europe. Additionally, the FDA has indicated that our Phase 3 clinical trials of Prophage Series R-100 (Oncophage) and M-200 cannot, by themselves, support BLA filings in the studies indications (renal cell carcinoma and metastatic melanoma). The signals and trends observed in these Phase 3 renal cell carcinoma and melanoma trials are based on data analysis of subgroups of patients, some of which were not pre-specified. While the subgroup data might be suggestive of treatment effect, under current regulatory guidelines the results cannot be expected, alone, to support registration or approval in the United States. Furthermore, regulatory authorities, including the FDA and the EMA, may have varying opinions of our product characterization, preclinical and clinical trial data for our other product candidates, which could delay, limit, or prevent regulatory approval or clearance. 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;
- diminish any competitive advantages that we or our licensees or collaborators may attain;
- limit our ability to receive royalties and generate revenue and profits; and
- adversely affect our business prospects and ability to obtain financing.

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

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

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

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

Failure to enter into significant licensing, distribution and/or collaboration agreements may hinder our efforts to develop and commercialize our product candidates and will increase our need to rely on other financing mechanisms, such as sales of debt or equity securities, to fund our operations.

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 or substantial royalty rates. 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.

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 Oncophage or any of the other Prophage Series vaccines. Due to the announcements in March 2006 that part I of our Phase 3 trial in renal cell carcinoma did not achieve its primary endpoint in the intent to treat population, and in November 2009 that the CHMP adopted a negative opinion on our MAA, and because companies may be skeptical regarding the potential success of a patient-specific product candidate, many companies may be unwilling to commit to an agreement prior to receipt of additional clinical data, if at all.

In addition, we would consider license and/or co-development opportunities to advance HerpV. This product is at an early stage and collaborative partners or licensees may defer discussions until results from early clinical trials become available, or they may not engage in such discussions at all. Further clinical development of HerpV will require a partner to support its advancement.

Because we rely on collaborators and licensees for the development and commercialization of some 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 some of our product candidates by continuing our existing arrangements with academic and corporate collaborators and licensees and by entering into new collaborations. Our success depends on our ability to negotiate such agreements and on the success of the other parties in performing research, preclinical and clinical testing, completing regulatory applications, and commercializing product candidates. For example, the development of Prophage G Series is currently dependent

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in large part on the efforts of our institutional collaborators, such as the Brain Tumor Research Center at the University of California, San Francisco, which is conducting Phase 2 clinical trials of Prophage Series G-100 and G-200 for the treatment of glioma. In addition, substantially all product candidates containing QS-21 depend on the success of our collaborative partners or licensees, and the Company s relationships with these third parties. Such product candidates depend on the successful and adequate manufacture and/or supply of QS-21, and 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.

These development activities 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. For example, an undisclosed infectious disease Phase 3 program has been discontinued by one of our collaborators, and in August 2006, Pharmexa A/S announced a decision to cease dosing patients in their Phase 2 clinical trial of their HER-2 Protein AutoVac breast cancer vaccine containing our QS-21 adjuvant, after it was determined that the trial was unlikely to meet its primary endpoint. Several of our agreements also require us to transfer important rights and regulatory compliance responsibilities to our collaborators and licensees. As a result of 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 devote resources to these arrangements 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 would increase our need to fund our operations through sales of debt or equity securities and would negatively affect our business prospects.

If we are unable to purify heat shock proteins we may have difficulty successfully initiating or completing our clinical trials, and, even if we do successfully complete our clinical trials, generating sizable market potential.

Depending on the type and stage of cancer and the patient population, our ability to successfully develop and commercialize the Prophage Series vaccines for a particular cancer depends in part on our ability to purify heat shock proteins from that type of cancer. If we experience difficulties in purifying heat shock proteins for a sufficiently large number of patients in our clinical trials, we may face delays in enrolling sufficient patients and subsequently utilize more internal resources to satisfy enrolment requirements. Manufacturing failures may also lower the probability of a successful analysis of the data from clinical trials and, ultimately, the ability to obtain regulatory approvals. We have successfully manufactured product across many different cancer types, however, the success 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 90% of the tumors received for patients enrolled in our ongoing clinical trials in glioma. We expect to continue to devote resources to allow for a better evaluation of tumor characteristics and screening methods in an attempt to increase manufacturing success rates.

We may encounter problems with other types of cancer or patients, such as pediatric patients, as we expand our research. If we cannot overcome these problems, the number of cancer types that our heat shock protein product candidates could treat would be limited. In addition, if we commercialize our heat shock protein 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.

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If we fail to sustain and further build our intellectual property rights, competitors will be able to take advantage of our research and development efforts to develop competing products.

If we are not able to protect our proprietary technology, trade secrets, and know-how, our competitors may use our inventions to develop competing products. We currently have exclusive rights to 73 issued United States patents and 117 issued foreign patents. We also have exclusive rights to 4 pending United States patent applications and 29 pending foreign patent applications. However, our patents may not protect us against our competitors. Our patent positions, and those of other pharmaceutical and biotechnology companies, are generally uncertain and involve complex legal, scientific, and factual questions. The standards which the United States Patent and Trademark Office uses to grant patents, and the standards which courts use to interpret patents, are not always applied predictably or uniformly and can change, particularly as new technologies develop. Consequently, the level of protection, if any, that will be provided by our patents if we attempt to enforce them, and they are challenged, is uncertain. In addition, the type and extent of patent claims that will be issued to us in the future is uncertain. Any patents that are issued may not contain claims that permit us to stop competitors from using similar technology.

Furthermore, the product development timeline for biotechnology products is lengthy and it is possible that our issued patents covering our product candidates in the United States and other jurisdictions may expire prior to commercial launch. In addition, because our patent on QS-21 composition of matter has already expired in virtually all territories, we are limited to protecting certain combinations of QS-21 with other adjuvants or formulations of QS-21 with other agents, e.g., excipients that improve performance of the compound. However, there is no guarantee that a third party would necessarily choose to use QS-21 in combination with such adjuvants or formulate it with the excipients covered by our patents. We are aware of at least one other party that makes a synthetic version of QS-21, claimed by such party to be equivalent in activity to natural QS-21, and has also developed derivatives of QS-21 which have shown biological activity.

In addition to our patented technology, we also rely on unpatented technology, trade secrets, and confidential information. We may not be able to effectively protect our rights to this technology or information. Other parties may independently develop substantially equivalent information and techniques or otherwise gain access to or disclose our technology. We generally require each of our employees, consultants, collaborators, and certain contractors to execute a confidentiality agreement at the commencement of an employment, consulting, collaborative, or contractual relationship with us. However, these agreements may not provide effective protection of our technology or information, or in the event of unauthorized use or disclosure, they may not provide adequate remedies.

We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights, and we may be unable to protect our rights in, or to use, our technology.

There has been substantial litigation and other proceedings regarding patent and other intellectual property rights in the pharmaceutical and biotechnology industries. We may become a party to patent litigation or other proceedings regarding intellectual property rights.

If we choose to go to court to stop someone else from using the inventions claimed in our patents, that individual or company has the right to ask a court to rule that our patents are invalid and should not be enforced against that third party. These lawsuits are expensive and would consume time and other resources even if we were successful in stopping the infringement of our patents. In addition, there is a risk that the court will decide that our patents are not valid and that we do not have the right to stop the other party from using the claimed inventions. There is also the risk that, even if the validity of our patents is upheld, the court will refuse to stop the other party on the grounds that such other party s activities do not infringe our patents.

We may not have rights under some patents or patent applications related to some of our existing and proposed products or processes. Third parties may own or control these patents and patent applications in the United States and abroad. Therefore, in some cases, such as those described below, in order to develop, use,

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manufacture, sell, or import some of our existing or proposed products, or develop or use some of our existing or proposed processes, we or our collaborators may choose to seek, or be required to seek, licenses under third-party patents issued in the United States and abroad, or those that might issue from United States and foreign patent applications. In such an event, we likely would be required to pay license fees or royalties or both to the licensor. If licenses are not available to us on acceptable terms, we or our collaborators may not be able to exploit these products or processes.

Furthermore, a third party may claim that we are using inventions covered by such third-party s patents or other intellectual property rights and may go to court to stop us from engaging in our normal operations and activities. These lawsuits are expensive. Some of our competitors may be able to sustain the cost of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. There is a risk that a court would decide that we are infringing the third-party s patents and would order us to stop the activities covered by the patents. In addition, there is a risk that a court will order us to pay the other party substantial damages for having violated the other party s patents. The biotechnology industry has produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. Moreover, patent holders sometimes send communications to a number of companies in related fields suggesting possible infringement, and we, like a number of biotechnology companies, have received such communications in the past and may receive others in the future. If we are sued for patent infringement, we would need to demonstrate that our products either do not infringe the patent claims of the relevant patent and/or that the patent claims are invalid, which we may not be able to do. Proving invalidity, in particular, is difficult, since it requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents.

If patent litigation or other proceeding is resolved against us, we or our licensees or collaborators may be enjoined from using, manufacturing, selling, or importing our products or processes without a license from the other party, and we may be held liable for significant damages. We may not be able to obtain any required licenses on commercially acceptable terms or at all.

Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to enter into collaborations with other entities, obtain financing, or compete in the marketplace. Patent litigation and other proceedings may also absorb significant management time and other resources.

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

We are a party to various license agreements under which we receive the right to practice and use important third-party patent rights and we may enter into additional licenses in the future. Our existing licenses impose, and we expect future licenses will impose, various diligence, milestone payment, royalty, insurance, and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license, in which event we might not be able to market any product that is covered by the licensed patents.

If we fail to retain the services of, and/or maintain positive relations with, key individuals and our employees, 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 with Pramod K. Srivastava, Ph.D., and has been and continues to be integral to building our company and developing our technology. If Dr. Armen severed 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

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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.

Dr. Srivastava currently has a consulting agreement with us pursuant to which he is retained to provide advice and services to Agenus from time to time. This agreement has an initial term ending March 31, 2011.

We also rely greatly on engaging and retaining other highly trained and experienced senior management and scientific and operations personnel and consultants. The competition for these and other qualified personnel in the biotechnology field is intense. In order to reduce our expenses, we have eliminated certain employee benefits, restructured our business, and reduced staffing levels. This restructuring has eliminated any redundancy in skills and capabilities in key areas. If we are not able to attract and retain qualified personnel, we may not be able to achieve our strategic and operational objectives.

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

Agenus, our Chairman and Chief Executive Officer, Garo H. Armen, Ph.D., and two investment banking firms that served as underwriters in our initial public offering were named as defendants in a federal civil class action lawsuit in the United States District Court for the Southern District of New York. Substantially similar actions were filed concerning the initial public offerings for more than 300 different issuers, and the cases were coordinated for pre-trial purposes as In re Initial Public Offering Securities Litigation, 21 MC 92. The suit alleges that the brokerage arms of the investment banking firms charged secret excessive commissions to certain of their customers in return for allocations of our stock in the offering. The suit also alleges that shares of our stock were allocated to certain of the investment banking firms customers based upon agreements by such customers to purchase additional shares of our stock in the secondary market. The parties have reached a global settlement of the litigation. Under the settlement, the insurers will pay the full amount of settlement share allocated to the defendants, and the defendants will bear no financial liability. Agenus and the other defendants will receive complete dismissals from the case. In October 2009, the Court entered an order granting final approval of the settlement, and subsequently judgment was entered. Various objectors have filed appeals. If for any reason the settlement does not become effective, we believe we have meritorious defenses to the claims and intend to defend the action vigorously. We are unable to predict the likelihood of an unfavorable outcome or estimate our potential liability, if any.

In addition, we may currently be, or may become involved in additional litigation. Any such litigation could be expensive in terms of out-of-pocket costs and management time, and the outcome of any such litigation is uncertain.

Our directors and officers insurance policies provide $30.0 million of coverage. This insurance coverage may not be sufficient to cover us for future claims.

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

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

- decreased demand for Oncophage or our product candidates;
- regulatory investigations;
- injury to our reputation;

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withdrawal of clinical trial volunteers;

costs of related litigation; and

substantial monetary awards to plaintiffs.

We manufacture the Prophage Series vaccines from a patient s cancer cells, and medical professionals must inject the vaccines into the same patient from which they were manufactured. A patient may sue us if a hospital, a shipping company, or we fail to deliver the removed cancer tissue or that patient s Prophage Series vaccine. We anticipate that the logistics of shipping will become more complex if the number of patients we treat increases and that shipments of tumor and/or Prophage Series vaccines may be lost, delayed, or damaged. Additionally, complexities unique to the logistics of commercial products may delay shipments and limit our ability to move commercial product in an efficient manner without incident. To date, we have obtained transportation insurance coverage for commercial Oncophage being shipped to Russia. We do not have any other insurance that covers loss of or damage to the Prophage Series vaccines or tumor material, and we do not know whether such insurance will be available to us at a reasonable price or at all. We have limited product liability coverage for use of our product candidates. Our product liability policy provides $10.0 million aggregate coverage and $10.0 million per occurrence coverage. This limited insurance coverage may be insufficient to fully cover us for future claims.

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

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

Although we believe that our current procedures and programs for handling, storage, and disposal of these materials comply with federal, state, and local laws and regulations, we cannot eliminate the risk of accidents involving contamination from these materials. Although we have limited pollution liability coverage ($2.0 million) and a workers compensation liability policy, we could be held liable for resulting damages in the event of an accident or accidental release, and such damages could be substantially in excess of any available insurance coverage and could substantially disrupt our business.

Risks Related to our Common Stock

The unaffiliated holders of certain convertible securities have the right to convert such securities into a substantial percentage of our outstanding common stock.

According to publicly filed documents, Mr. Brad M. Kelley beneficially owns 5,546,240 shares of our outstanding common stock and 31,620 shares of our series A convertible preferred stock. The shares of preferred stock are currently convertible at any time into 2,000,000 shares of common stock at an initial conversion price of $15.81, are non-voting, and carry a 2.5% annual dividend yield. If Mr. Kelley had converted all of the shares of preferred stock on December 31, 2010, he would have held approximately 7% of our outstanding common stock. We currently have a right of first refusal agreement with Mr. Kelley that provides us with limited rights to purchase certain of Mr. Kelley s shares if he proposes to sell them to a third party.

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Mr. Kelley s substantial ownership position provides him with the ability to substantially influence the outcome of matters submitted to our stockholders for approval. Furthermore, collectively, Mr. Kelley and Garo Armen, our CEO, control approximately 11% of our outstanding common stock as of December 31, 2010, providing ability, if they vote in the same manner, to determine the outcome of matters submitted to a stockholder vote. If Mr. Kelley were to convert all of his preferred stock into common stock, the combined total would increase to 12%. Additional purchases of our common stock by Mr. Kelley also would increase both his percentage of outstanding voting rights and the percentage combined with our CEO. While Mr. Kelley s shares of preferred stock do not carry voting rights, the shares of common stock issuable upon conversion carry the same voting rights as other shares of common stock.

Our stock may be delisted from the Nasdaq Capital Market, which could affect its market price and liquidity.

Our common stock is currently listed on the Nasdaq Capital Market under the symbol AGEN. In the event that we fail to satisfy any of the listing requirements, our common stock may be put under review or removed from the listing on the Nasdaq Capital Market.

On March 3, 2011, we were notified by the Listing Qualifications Staff of Nasdaq (the Staff) indicating that we are not in compliance with the 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. In accordance with Nasdaq Marketplace Rule 5810(c)(3)(A), we have been provided 180 calendar days, or until August 30, 2011, to regain compliance with the Bid Price Requirement.

If compliance is not demonstrated within the applicable compliance period, the Staff will notify us that our securities will be delisted from the Nasdaq Capital Market. However, we may appeal the Staff s determination to delist our securities to a Hearings Panel. During any appeal process, shares of our common stock would continue to trade on the Nasdaq Capital Market. There can be no assurance that we will meet the requirements for continued listing on the Nasdaq Capital Market or whether any appeal would be granted by the Hearings Panel.

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

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

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

Between our initial public offering on February 4, 2000 and December 31, 2010, and for the year ended December 31, 2010, the closing price of our common stock has fluctuated between $0.30 and $52.63 per share and $0.60 and $1.38 per share, respectively. The average daily trading volume for the year ended December 31, 2010 was approximately 1,103,000 shares. The market may experience significant price and volume fluctuations that are often unrelated to the operating performance of individual companies. In addition to general market volatility, many factors may have a significant adverse effect on the market price of our stock, including:

- continuing operating losses, which we expect over the next several years as we continue our development activities;
- announcements of decisions made by public officials;
- results of our preclinical studies and clinical trials;
- announcements of new collaboration agreements with strategic partners or developments by our existing collaborative partners;
- announcements of technological innovations, new commercial products, failures of products, or progress toward commercialization by our competitors or peers;
- developments concerning proprietary rights, including patent and litigation matters;
- publicity regarding actual or potential results with respect to product candidates under development; and
- quarterly fluctuations in our financial results.

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

The sale by us or the resale by stockholders of a significant number of shares of our common stock could cause the market price of our common stock to decline. As of December 31, 2010, we had approximately 111,625,000 shares of common stock outstanding. All of these shares are eligible for sale on the Nasdaq Capital Market, although certain of the shares are subject to sales volume and other limitations. We have filed registration statements to permit the sale of approximately 25,437,000 shares of common stock under our equity incentive plan and certain equity plans that we assumed in our acquisitions of Aquila Biopharmaceuticals, Inc. and Aronex Pharmaceuticals, Inc. We have also filed registration statements to permit the sale of 1,000,000 shares of common stock under our employee stock purchase plan, to permit the sale of 450,000 shares of common stock under our Directors Deferred Compensation Plan, to permit the sale of 49,643,966 shares of common stock pursuant to various private placement agreements. As of December 31, 2010, an aggregate of 39.3 million shares remain available for sale under these registration statements. The market price of our common stock may decrease based on the expectation of such sales.

As of December 31, 2010, options to purchase 7,272,850 shares of our common stock with a weighted average exercise price per share of $2.24 were outstanding. Many of these options are subject to vesting that generally occurs over a period of up to four years following the date of grant. As of December 31, 2010, we have 513,449 nonvested shares outstanding.

Because we are a small public company we believe we have been disproportionately negatively impacted by the Sarbanes-Oxley Act of 2002 and related regulations which have increased our costs in the past and have required additional management resources.

The Sarbanes-Oxley Act of 2002 and rules adopted by the SEC and the Nasdaq have resulted in significant costs to us. In particular, our efforts to comply with Section 404 of the Sarbanes-Oxley Act of 2002 and related regulations regarding the required assessment of our internal control over financial reporting, and our

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independent registered public accounting firm s audit of internal control over financial reporting, have required commitments of significant management time. We expect these commitments to continue. Additionally, these laws and regulations could make it more difficult for us to attract and retain qualified members for our Board of Directors, particularly independent directors, or qualified executive officers.

Our internal control over financial reporting (as defined in Rules 13a-15 of the Securities Exchange Act) is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our consolidated financial statements for external purposes in accordance with U.S. generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect all deficiencies or weaknesses in our financial reporting. While our management has concluded that there were no material weaknesses in our internal control over financial reporting as of December 31, 2010, our procedures are subject to the risk that our controls may become inadequate because of changes in conditions or as a result of a deterioration in compliance with such procedures. No assurance is given that our procedures and processes for detecting weaknesses in our internal control over financial reporting will be effective.

Item 1B. ***Unresolved Staff Comments***

We have received no written comments from the staff of the SEC regarding our periodic or current reports that (1) we believe are material, (2) were issued not less than 180 days before the end of our 2010 fiscal year, and (3) remain unresolved.

Item 2. ***Properties***

We maintain our corporate offices in Lexington, Massachusetts, in a 162,000 square foot facility under a lease agreement that terminates in August 2013. We have an option to renew this lease for two additional ten-year periods. We have sublet a portion of this facility.

In addition, we leased approximately 40,000 square feet of laboratory, office, and manufacturing space in Framingham, Massachusetts under a lease agreement that terminated in September 2010. We had sublet this entire facility.

We also lease approximately 5,400 square feet in an office building in New York, New York. Our New York lease terminates in April 2012.

We believe substantially all of our property and equipment is in good condition and that we have sufficient capacity to meet our current operational needs. We do not anticipate experiencing significant difficulty in retaining occupancy of any of our manufacturing or office facilities and will do so through lease renewals prior to expiration or through replacing them with equivalent facilities.

Item 3. ***Legal Proceedings***

Agenus, our Chairman and CEO, Garo H. Armen, Ph.D., and two investment banking firms that served as underwriters in our initial public offering were named as defendants in a federal civil class action lawsuit in the United States District Court for the Southern District of New York. Substantially similar actions were filed concerning the initial public offerings for more than 300 different issuers, and the cases were coordinated for pre-trial purposes as In re Initial Public Offering Securities Litigation, 21 MC 92. The suit alleges that the brokerage arms of the investment banking firms charged secret excessive commissions to certain of their customers in return for allocations of our stock in the offering. The suit also alleges that shares of our stock were allocated to certain of the investment banking firms customers based upon agreements by such customers to purchase additional shares of our stock in the secondary market. The parties have reached a global settlement of the litigation. Under the settlement, the insurers will pay the full amount of settlement share allocated to the defendants, and the defendants will bear no financial liability. Agenus and the other defendants will receive complete dismissals from the case. In October 2009, the Court entered an order granting final approval of the

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settlement, and subsequently judgment was entered. Various objectors have filed appeals. If for any reason the settlement does not become effective, we believe we have meritorious defenses to the claims and intend to defend the action vigorously. We are unable to predict the likelihood of an unfavorable outcome or estimate our potential liability, if any.

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

Item 4. ***(Removed and Reserved)***

Executive Officers of the Registrant

Set forth below is certain information regarding our current and certain former executive officers, including their age, as of March 1, 2011:

Name	Age	Title
Garo H. Armen, Ph.D.	58	Chairman of the Board and Chief Executive Officer
Shalini Sharp	36	Vice President and Chief Financial Officer
Christine M. Klaskin	45	Vice President, Finance and Principal Accounting Officer
Karen H. Valentine	39	Vice President and General Counsel
Kerry A. Wentworth	38	Vice President, Clinical, Regulatory & Quality

Garo H. Armen, PhD Dr. Armen is Chairman and Chief Executive Officer of Agenus Inc., the biotechnology company he co-founded with Pramod Srivastava in 1994. From mid-2002 through 2004, he was Chairman of the Board of Directors for the biopharmaceutical company Elan Corporation, plc. Dr. Armen is also the founder and President of the Children of Armenia Fund, a charitable organization established in 2000 that is dedicated to the positive development of the children and youth of Armenia.

Shalini Sharp Ms. Sharp is Chief Financial Officer of Agenus Inc. Prior to joining Agenus Inc. in 2003, Ms. Sharp was director of strategic planning at Elan Corporation, plc., where she served as chief of staff to the chairman of the board during the restructuring process and drove to completion a number of strategic corporate and financial transactions. Ms. Sharp was previously a management consultant at McKinsey & Company, specializing in pharmaceuticals and medical devices. Ms. Sharp received her BA and MBA from Harvard University.

Christine M. Klaskin Christine M. Klaskin is Vice President, Finance and Principal Accounting Officer. Since joining Agenus Inc. in 1996 as finance manager, Ms. Klaskin has held various positions within the finance department and has been involved in all equity and debt offerings of the Company including its IPO. Prior to joining Agenus, Ms. Klaskin was employed by Arthur Andersen as an audit manager. Ms. Klaskin received her Bachelor of Accountancy from The George Washington University.

Karen H. Valentine Karen Higgins Valentine is Vice President and General Counsel and also serves as Secretary and Chief Compliance Officer of the Company. Prior to joining Agenus Inc. in 2004, Ms. Valentine was an associate in the biotechnology practice of Palmer & Dodge LLP (now Edwards, Angell, Palmer & Dodge LLP). While at the law firm, she provided corporate law services to a broad range of both public and private corporations, and developed an expertise in the areas of licensing and strategic collaborations. Ms. Valentine graduated cum laude with a bachelor s degree in neuroscience from Colgate University, and received her law degree, magna cum laude, from Boston University School of Law.

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Kerry A. Wentworth Kerry Wentworth is Vice President, Clinical, Regulatory & Quality. Before joining Agenus Inc. in 2005, Ms. Wentworth served as senior director of regulatory affairs at Genelabs Technologies, where she was responsible for the business regulatory and quality functions. There she focused on the late-stage clinical development and subsequent US and European commercial application filings for the company s lead product Prestara. Prior to Genelabs, Ms. Wentworth held various positions in regulatory affairs at Shaman Pharmaceuticals and at Genzyme Corporation. Ms. Wentworth received a BS in pre-veterinary medicine from the University of New Hampshire.

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PART II

Item 5. ***Market for Registrant s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities***

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

The following table sets forth, for the periods indicated, the high and low sale prices per share of our common stock.

	High	Low
2009		
First Quarter	$ 0.60	$ 0.19
Second Quarter	3.34	0.43
Third Quarter	3.11	1.46
Fourth Quarter	2.24	0.63
2010		
First Quarter	1.20	0.60
Second Quarter	1.72	0.70
Third Quarter	1.12	0.73
Fourth Quarter	1.12	0.87

As of March 1, 2011, there were approximately 1,900 holders of record and approximately 25,000 beneficial holders of our common stock.

We have never paid cash dividends on our common stock, and we do not anticipate paying any cash dividends in the foreseeable future. We currently intend to retain future earnings, if any, for the future operation and expansion of our business. Any future payment of dividends on our common stock will be at the discretion of our Board of Directors and will depend upon, among other things, our earnings, financial condition, capital requirements, level of indebtedness, and other factors that our Board of Directors deems relevant.

Stock Performance

The following graph shows the cumulative total stockholder return on our common stock over the period from December 31, 2005 to December 31, 2010, as compared with that of the Nasdaq Stock Market (U.S. Companies) Index and the Nasdaq Biotechnology Index, based on an initial investment of $100 in each on December 31, 2005. Total stockholder return is measured by dividing share price change plus dividends, if any, for each period by the share price at the beginning of the respective period, and assumes reinvestment of dividends.

This stock performance graph shall not be deemed filed with the SEC or subject to Section 18 of the Securities Exchange Act, nor shall it be deemed incorporated by reference in any of our filings under the Securities Act of 1933, as amended (the Securities Act).

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COMPARISON OF CUMULATIVE TOTAL RETURN OF AGENUS INC.,

NASDAQ STOCK MARKET (U.S. COMPANIES) INDEX

AND NASDAQ BIOTECHNOLOGY INDEX

	12/31/2005	12/31/2006	12/31/2007	12/31/2008	12/31/2009	12/31/2010
Agenus Inc.	100.00	38.45	42.86	10.08	13.45	21.22
NASDAQ Stock Market (U.S. Companies) Index	100.00	109.52	120.27	71.51	102.89	120.29
NASDAQ Biotechnology Index	100.00	101.02	105.65	92.31	106.74	122.76

Recent Sales of Unregistered Securities

The below listed payments in 2008 relate to compensation to a third-party consultant, Raifarm Limited or its affiliates (collectively, Raifarm), for services rendered in relation to the registration and commercialization activities in Russia for Oncophage pursuant to a Master Services Agreement between us and Raifarm, as amended from time to time. The below listed payments in 2010 relate to compensation to a third-party consultant, Hamilton Communications (Hamilton), for services rendered in connection with our rebranding effort pursuant to a Services Agreement between us and Hamilton, as amended. The offer, issuance and delivery of the below listed shares of common stock in the manner contemplated by the applicable agreements, did not require registration under Section 5 of the Securities Act because the transactions were exempted transactions under Section 4(2) of the Securities Act. This determination was based upon and assuming the accuracy of representations and warranties we obtained from Raifarm and Hamilton and compliance by Raifarm and Hamilton with the offering and transfer procedures and restrictions described in the applicable agreements and related documents.

Date Issued	Title of Each Class of Security	Amount of Securities Amount Issued	Nature of Transaction Nature of Transaction
Various dates, February July, 2008	Common Stock, par value $0.01	346,509	Shares issued for services rendered
September 16, 2010	Common Stock, par value $0.01	111,111	Shares issued for services rendered
November 30, 2010	Common Stock, par value $0.01	54,945	Shares issued for services rendered

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Information concerning our equity compensation plans is set forth in our Definitive Proxy Statement with respect to our 2011 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission no later than 120 days after the end of the fiscal year under the heading Equity Plans, which is incorporated herein by reference.

Item 6. ***Selected Financial Data***

We have derived the consolidated balance sheet data set forth below as of December 31, 2010 and 2009, and the consolidated statement of operations data for each of the years in the three-year period ended December 31, 2010, from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

You should read the selected consolidated financial data in conjunction with Management s Discussion and Analysis of Financial Condition and Results of Operations, our consolidated financial statements, and the notes to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Given our history of incurring operating losses, management believes that it is more likely than not that any deferred tax assets will not be realized through future earnings. Therefore, no income tax benefit has been recognized in the consolidated statements of operations because of the loss before income taxes, and the need to recognize a valuation allowance on the portion of our deferred tax assets, which will not be offset by the reversal of deferred tax liabilities (see Note (1) below).

Changes in cash, cash equivalents, and short-term investments, total current assets, total assets, and stockholders deficit in the periods presented below include the effects of the receipt of net proceeds from our debt offerings, equity offerings, the exercise of stock options and warrants, and employee stock purchases that totaled approximately $11.6 million, $18.7 million, $46.9 million, $4.6 million, and $25.4 million in the years ended December 31, 2010, 2009, 2008, 2007, and 2006, respectively.

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	For the Year Ended December 31,				
	2010	2009	2008	2007	2006
	(In thousands, except per share data)				
Consolidated Statement of Operations Data:					
Revenue	$ 3,360	$ 3,334	$ 2,651	$ 5,552	$ 692
Operating expenses:					
Cost of goods sold	(123)				
Research and development	(12,878)	(16,903)	(20,663)	(21,789)	(28,643)
General and administrative	(12,112)	(14,110)	(19,832)	(17,041)	(21,288)
Restructuring costs					(1,374)
Loss from operations	(21,753)	(27,679)	(37,844)	(33,278)	(50,613)
Non-operating income	4,680	2,568	12,356	1	141
Interest expense, net	(4,834)	(5,207)	(5,313)	(4,658)	(2,287)
Net loss (1)	(21,907)	(30,318)	(30,801)	(37,935)	(52,759)
Dividends on series A convertible preferred stock	(790)	(790)	(790)	(790)	(790)
Net loss attributable to common stockholders	$ (22,697)	$ (31,108)	$ (31,591)	$ (38,725)	$ (53,549)
Net loss attributable to common stockholders per common share, basic and diluted	$ (0.23)	$ (0.39)	$ (0.50)	$ (0.83)	$ (1.17)
Weighted average number of shares outstanding, basic and diluted	96,650	79,017	63,249	46,512	45,809

	December 31,				
	2010	2009	2008	2007	2006
	(In thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents, and short-term investments	$ 19,782	$ 30,065	$ 34,463	$ 18,679	$ 40,095
Total current assets	20,854	31,533	35,486	20,782	42,298
Total assets	30,907	45,874	56,822	44,351	72,726
Total current liabilities	5,416	5,355	6,997	8,383	9,078
Long-term debt, less current portion	34,050	49,494	64,126	71,524	68,276
Stockholders deficit	(14,707)	(16,975)	(20,330)	(41,370)	(10,563)

(1) Given our history of incurring operating losses, no income tax benefit has been recognized in our consolidated statements of operations because of the loss before income taxes, and the need to recognize a valuation allowance on the portion of our deferred tax assets which will not be offset by the reversal of deferred tax liabilities.

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Item 7. ***Management s Discussion and Analysis of Financial Condition and Results of Operations***

Overview

Our current research and/or development activities are focused on developing technologies and product candidates to treat cancers and infectious diseases. Since our inception in March 1994, our activities have primarily been associated with the development of our heat shock protein technology, primarily our lead autologous cancer immunotherapies (formerly referred to as Oncophage), the Prophage Series of cancer vaccines (vitespen; HSPPC-96). The first product derived from the Prophage Series of vaccines (R-100, still referred to in Russia and Europe as Oncophage), represents the only approved treatment for adjuvant or non-metastatic renal cell carcinoma (RCC; kidney cancer) patients at intermediate risk for disease 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 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). 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. Additional trials are planned in metastatic RCC (R-200) and metastatic melanoma (M-200) in combination with potentially synergistic therapies, as well as in pediatric neurological tumors (NP-150). Our business activities have included product research and development, intellectual property prosecution, manufacturing, regulatory and clinical affairs, corporate finance and development, market development, and support of our collaborations.

We have incurred significant losses since our inception. As of December 31, 2010, we had an accumulated deficit of $584.4 million. Since our inception, we have financed our operations primarily through the sale of equity and convertible notes, interest income earned on cash, cash equivalents, and short-term investment balances, and debt provided through secured lines of credit. We believe that, based on our current plans and activities, our working capital resources at December 31, 2010, anticipated revenues, and the estimated proceeds from our license, supply, and collaborative agreements will be sufficient to satisfy our liquidity requirements through 2011. We expect to attempt to raise additional funds in advance of depleting our current funds. We may attempt to raise additional funds by: (1) licensing technologies or products to one or more collaborative partners, (2) renegotiating third party agreements, (3) completing an outright sale of assets, (4) securing additional debt financing, and/or (5) selling additional equity securities. Satisfying long-term liquidity needs may require the successful commercialization of (1) our product, Oncophage and/or one or more partnering arrangements for Oncophage, (2) vaccines containing QS-21 under development by our licensees, and/or (3) potentially other product candidates, each of which will require additional capital.

In April 2008, the Russian Ministry of Public Health issued a registration certificate for the use of Oncophage for the adjuvant treatment of kidney cancer patients at intermediate risk for disease recurrence and, in September 2008, the Food & Drug Administration (FDA) granted the necessary permission to allow for the export of Oncophage from the United States for patient administration in Russia. 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 October 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 this MAA. Subsequently we withdrew our application and we have been evaluating a variety of options to potentially bring Oncophage to patients and physicians globally. 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 Prophage Series.

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Guidance received from past interaction with the FDA indicated that an additional Phase 3 clinical study must be conducted to demonstrate the efficacy and safety of Oncophage. Because the primary evidence of efficacy comes from a subgroup analysis of the pre-specified primary and secondary endpoints and was not demonstrated in the intent-to-treat population, our Phase 3 renal cell carcinoma trial is likely not sufficient as sole support for product approval based on existing standards in the United States and potentially in other territories.

On March 3, 2011, we were notified by the Listing Qualifications Staff of Nasdaq (the Staff) indicating that we are not in compliance with the Bid 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. In accordance with Nasdaq Marketplace Rule 5810(c)(3)(A), we have been provided 180 calendar days, or until August 30, 2011, to regain compliance with the Bid Price Requirement. If compliance is not demonstrated within the applicable compliance period, the Staff will notify us that our securities will be delisted from the Nasdaq Capital Market. However, we may appeal the Staff s determination to delist our securities to a Hearings Panel. During any appeal process, shares of our common stock would continue to trade on the Nasdaq Capital Market. There can be no assurance that we will meet the requirements for continued listing on the Nasdaq Capital Market or whether any appeal would be granted by the Hearings Panel.

Historical Results of Operations

Year Ended December 31, 2010 Compared to the Year Ended December 31, 2009

Revenue: We generated revenue of $3.4 million and $3.3 million during the years ended December 31, 2010 and 2009, respectively. Revenue includes revenue earned on shipments of QS-21 to our QS-21 licensees, license fees, royalties earned, and in 2010, grants earned and Oncophage sales. In the years ended December 31, 2010 and 2009, we recorded $1.5 million each period from the amortization of deferred revenue related to our QS-21 partnered programs.

Research and Development: Research and development expenses include the costs associated with our internal research and development activities, including compensation and benefits, occupancy costs, clinical manufacturing costs, costs of consultants, and administrative costs. Research and development expense decreased 24% to $12.9 million for the year ended December 31, 2010 from $16.9 million for the year ended December 31, 2009. The decrease included declines of $1.7 million for personnel related expenses and $367,000 for facility related costs primarily due to cost containment efforts, and $1.8 million for various outside services primarily related to the status of our efforts in Russia and other territories.

General and Administrative: General and administrative expenses consist primarily of personnel costs, facility expenses, and professional fees. General and administrative expenses decreased 14% to $12.1 million for the year ended December 31, 2010 from $14.1 million for the year ended December 31, 2009. This decrease is largely attributable to declines of $1.5 million for various outside services primarily relating to the status of our efforts in Russia and other territories, and $145,000 in employee and director noncash share-based compensation expense.

Non-operating Income: Non-operating income of $4.7 million for the year ended December 31, 2010 consists of a net gain of $2.8 million on the extinguishment of a portion of our 2005 Notes and the change in the fair value of our derivative liability since December 31, 2009 of $1.9 million.

Interest Expense: Interest expense decreased to $4.9 million for the year ended December 31, 2010 from $5.3 million for the year ended December 31, 2009. This decrease is related to the repurchase of a portion of our 2005 Notes. Interest on our 2006 Notes is payable semi-annually on December 30 and June 30 in cash or, at our option, in additional notes or a combination thereof. During the years ended December 31, 2010 and 2009, interest expense included $2.6 million and $2.4 million, respectively, paid in the form of additional 2006 Notes.

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Interest Income: Interest income decreased 73% to $38,000 for the year ended December 31, 2010 from $137,000 for the year ended December 31, 2009. This decrease is primarily attributable to a decrease in our average cash, cash equivalents and short-term investments balance coupled with declining interest rates earned on our cash, cash equivalents, and short-term investments. Our average interest rate earned decreased from 0.49% for the year ended December 31, 2009 to 0.15% for the year ended December 31, 2010.

Year Ended December 31, 2009 Compared to the Year Ended December 31, 2008

Revenue: We generated revenue of $3.3 million and $2.7 million during the years ended December 31, 2009 and 2008, respectively. Revenue includes revenue earned on shipments of QS-21 to our QS-21 licensees, license fees, and royalties earned. In the years ended December 31, 2009 and 2008, we recorded $1.5 million each period from the amortization of deferred revenue related to our QS-21 partnered programs.

Research and Development: Research and development expenses include the costs associated with our internal research and development activities, including compensation and benefits, occupancy costs, clinical manufacturing costs, costs of consultants, and administrative costs. Research and development expense decreased 18% to $16.9 million for the year ended December 31, 2009 from $20.7 million for the year ended December 31, 2008. The decrease included declines of $1.5 million for personnel related expenses and $241,000 for facility related costs primarily due to cost containment efforts, and $1.5 million for various outside services primarily related to the status of our efforts in Russia and other territories.

General and Administrative: General and administrative expenses consist primarily of personnel costs, facility expenses, and professional fees. General and administrative expenses decreased 29% to $14.1 million for the year ended December 31, 2009 from $19.8 million for the year ended December 31, 2008. This decrease is largely attributable to declines of $2.3 million for various outside services primarily relating to the status of our efforts in Russia and other territories, $1.5 million in personnel related expenses due to cost containment efforts, $1.0 million in employee and director noncash share-based compensation expense and a $332,000 decrease in our foreign currency exchange loss.

Non-operating Income: Non-operating income of $2.6 million for the year ended December 31, 2009 consists primarily of a gain on the extinguishment of a portion of our 2005 Notes.

Interest Expense: Interest expense decreased to $5.3 million for the year ended December 31, 2009 from $6.3 million for the year ended December 31, 2008. This decrease is related to the repurchase of a portion of our 2005 Notes during the fourth quarter of 2008 and the second quarter of 2009. Interest on our 2006 Notes is payable semi-annually on December 30 and June 30 in cash or, at our option, in additional notes or a combination thereof. During the years ended December 31, 2009 and 2008, interest expense included $2.4 million and $2.2 million, respectively, paid in the form of additional 2006 Notes.

Interest Income: Interest income decreased 86% to $137,000 for the year ended December 31, 2009 from $966,000 for the year ended December 31, 2008. This decrease is primarily attributable to a decrease in our average cash, cash equivalents and short-term investments balance coupled with declining interest rates earned on our cash, cash equivalents, and short-term investments. Our average interest rate earned decreased from 2.4% for the year ended December 31, 2008 to 0.49% for the year ended December 31, 2009.

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Research and Development Programs

Prior to 2002, we did not track costs on a per project basis, and therefore have estimated the allocation of our total research and development costs to our largest research and development programs for that time period. During 2010, these research and development programs consisted largely of our Prophage Series vaccines and QS-21, as indicated in the following table (in thousands).

Research and Development Program	Product	Year Ended December 31, 2010	2009	2008	Prior to 2008	Total
Heat shock proteins for cancer	Prophage Series Vaccines	$ 10,960	$ 15,309	$ 17,156	$ 238,426	$ 281,851
Heat shock proteins for infectious diseases	HerpV	644	262	1,377	16,071	18,354
Vaccine adjuvant *	QS-21	1,185	1,071	648	9,500	12,404
Other research and development programs		89	261	1,482	31,695	33,527
Total research and development expenses		$ 12,878	$ 16,903	$ 20,663	$ 295,692	$ 346,136

* Prior to 2000, costs were incurred by Aquila Biopharmaceuticals, Inc., a company we acquired in November 2000.

Research and development program costs include compensation and other direct costs plus an allocation of indirect costs, based on certain assumptions and our review of the status of each program. Our Prophage Series vaccines are in various stages of development as described below. Significant additional expenditures will be required if we start new trials, encounter delays in our programs, apply for regulatory approvals, continue development of our technologies, expand our operations, and/or bring our product candidates to market. The eventual total cost of each clinical trial is dependent on a number of factors such as trial design, length of the trial, number of clinical sites, and number of patients. The process of obtaining and maintaining regulatory approvals for new therapeutic products is lengthy, expensive, and uncertain. Because the further development of our Prophage Series vaccines is subject to evaluation and uncertainty, and because HerpV is an early-stage clinical development candidate and generally on hold due to cost-containment efforts, we are unable to reliably estimate the cost of completing our research and development programs, the timing of bringing such programs to various markets, and, therefore, when, if ever, material cash inflows are likely to commence. Programs involving QS-21 depend on our collaborative partners or licensees successfully completing clinical trials, successfully manufacturing QS-21 to meet demand, obtaining regulatory approvals and successfully commercializing product candidates containing QS-21.

Product Development Portfolio

Prophage Series of Cancer Vaccines

We started enrolling patients in our first clinical trial studying a Prophage Series vaccine at Memorial Sloan-Kettering Cancer Center in New York, New York in November 1997. To date, we have treated nearly 850 cancer patients in our clinical trials. Because Prophage Series vaccines are novel therapeutic vaccines that are patient-specific, meaning derived from the patient s own tumor, they are experiencing a long development process and 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 under Part I-Item 1A. Risk Factors of this Annual Report on Form 10-K.

We believe that the collective results from our clinical trials thus far show that the Prophage Series vaccines have a favorable safety profile. We also believe that available results from clinical trials suggest that treatment with Prophage Series vaccines can generate immunological and anti-tumor responses.

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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 showed a statistically significant difference in recurrence-free survival in favor of the Oncophage arm. In part because the intermediate-risk category was not prospectively delineated prior to the trial s initiation, the 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.

We opened a subsequent protocol that continued to follow patients from this trial in the format of a registry in order to collect overall survival information, as well as investigator reports of disease recurrence. The registry, which is expected to provide additional data on the effectiveness of the vaccine, followed patients until March 2010, an additional three years from closure of the initial trial, providing more than five years of data collection following the enrollment of the last patient in the trial. Final analysis of this data is in process. At the 2009 American Society of Clinical Oncology (ASCO) annual meeting, we announced results of an interim analysis from the ongoing global patient survival registry, which showed that patients with kidney cancer at intermediate risk of disease recurrence demonstrated an approximately 46 percent lower risk of death in the treatment arm compared with the control arm (n = 362; $P < 0.05$; hazard ratio = 0.54).

In addition to the patient registry, patient enrollment has commenced into a small study in non-metastatic RCC to assess immune response in the intermediate-risk patient population. The results of this study, continued data collection through the survival registry, and ongoing analysis are uncertain, and may not positively affect the acceptability of the overall results of the trial and, even if clinically meaningful, may not meet the requirements of the FDA or other regulatory authorities for submission and approval of a marketing application or similar applications for product approval outside the United States.

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 during the year ended December 31, 2010. 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. Since this approval we have been focusing our efforts in Russia on securing one or more distribution and/or partnering arrangements and related commercialization activities. The amount of any future revenue generated from the sale of Oncophage in Russia will depend on our ability to successfully execute on these efforts and identify and obtain adequate reimbursement, as well as on decisions of physicians and patients, among other factors. Furthermore, we may experience significant delays in the receipt of payment for Oncophage, or an inability to collect payments at all.

In October 2008, we announced the submission of a MAA to the EMA requesting conditional authorization of Oncophage in earlier-stage, localized kidney cancer. On November 20, 2009, we announced that the CHMP of the EMA formally adopted a negative opinion on this MAA. Subsequently we withdrew our application and have been evaluating a variety of options to potentially bring Oncophage to patients and physicians globally. 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.

A Phase 2 clinical trial with Prophage Series G-200 vaccine 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

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Special Programs of Research Excellence. Phase 1 results, presented at the Society for Neuro-Oncology Annual Meeting Conference in November 2008, showed that vaccination following brain cancer surgery increased overall median survival to approximately 10.5 months, with four patients surviving beyond 12 months and one patient surviving almost 2.5 years. The study also showed that all 12 treated patients demonstrated a significant immune response after vaccination with G-200 ($P < 0.001$) and that patients with minimal residual disease at time of first vaccination (n = 7) were more likely to survive beyond nine months compared with patients with significant residual disease.

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. Interim data was presented at the Society for Neuro-Oncology meeting in October 2009, which showed a median survival of 10.1 months in the first 20 patients treated with G-200, and that to date six patients (30 percent) had survived at or beyond 12 months. This early data shows an improvement in overall survival over the previous long-standing historical median survival of 6.5 months, and is also slightly favorable to the recently reported median survival of 9.2 months with Avastin® (bevacizumab) in patients with recurrent high-grade glioma. In May 2010, data presented at the International Conference on Brain Tumor Research and Therapy suggested that vaccination with this candidate may improve overall survival in patients with recurrent high-grade glioma. An overall median survival of 44 weeks after tumor resection was observed. Approximately 70% of the evaluable patients survived beyond 36 weeks, and 41% survived up to or longer than one year. Additional data from this trial will be reported by mid-2011. UCSF also initiated an additional Phase 2 clinical trial in newly diagnosed glioma testing Prophage Series G-100 vaccine in combination with Temodar® (temozolomide). This trial is currently enrolling, with a target of 50 patients. Based on promising trends to date, this trial is being expanded to include up to 10 clinical sites.

QS-21

QS-21 Stimulon® adjuvant 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 Alzheimer Immunotherapy. There are 14 vaccines containing QS-21 in clinical development, including four in Phase 3 testing for malaria, melanoma, non-small cell lung cancer and shingles. The first products containing QS-21 are expected to be launched in the 2013-2014 timeframe. 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. The Company does not incur clinical development costs for these products and is generally reimbursed for any related expenses by its licensees.

In return for rights to use QS-21, our licensees 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. From time to time our collaborators or licensees initiate and/or cease programs containing QS-21. For example, an undisclosed infectious disease Phase 3 program was recently discontinued by one of our collaborators.

On January 16, 2009, we entered into an Amended and Restated Manufacturing Technology Transfer and 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. We understand that QS-21 is a key component included in several of GSK s proprietary adjuvant systems and that a number of GSK s vaccine candidates currently under development are formulated using adjuvant systems containing QS-21. GSK has initiated Phase 3 studies evaluating its investigational MAGE-A3 Antigen-Specific Cancer Immunotherapeutic containing QS-21 in non-small cell lung cancer and melanoma. GSK has also initiated a Phase 3 clinical trial in malaria and a Phase 3 clinical trial in shingles. Revenues recognized with respect to this agreement were $1.3 million for each of the years ended December 31, 2010 and 2009.

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Elan Pharmaceuticals, Inc. and/or its affiliates (Elan) had a commercial license for the use of QS-21 in the research and commercialization of products. Effective September 14, 2009, we entered into an Amended and Restated License Agreement (Amended License Agreement) with Elan. On September 17, 2009, the Amended License Agreement was assigned to JANSSEN Alzheimer Immunotherapy. Under the terms of the Amended License Agreement assigned to JANSSEN Alzheimer Immunotherapy, they will have the right to develop, make, have made, use, sell, offer for sale, import, and have sold, the Alzheimer s disease vaccine that contains QS-21 (Licensed Product). In addition, pursuant to the terms of the Amended License Agreement, JANSSEN Alzheimer Immunotherapy 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. Under the terms of the Amended License Agreement, we are entitled to receive future milestone payments and product royalties in the event of the successful development of the Licensed Product. In 2007, Elan initiated a Phase 2 study of their vaccine. Revenues recognized with respect to this agreement were $160,000 in the year ended December 31, 2010.

Liquidity and Capital Resources

We have incurred annual operating losses since inception, and we had an accumulated deficit of $584.4 million as of December 31, 2010. We expect to incur significant losses over the next several years as we continue our clinical trials, apply for regulatory approvals, prepare for commercialization, and continue development of our technologies. Since our inception, we have financed our operations primarily through the sale of equity and convertible notes, interest income earned on cash, cash equivalents, and short-term investment balances, and debt provided through secured lines of credit. From our inception through December 31, 2010, we have raised aggregate net proceeds of $506.3 million through the sale of common and preferred stock, the exercise of stock options and warrants, proceeds from our employee stock purchase plan, and the issuance of convertible notes, and borrowed $20.5 million under two credit facilities. During February 2010, we entered into an At the Market Sales Agreement with McNicoll, Lewis & Vlak LLC and Wm Smith & Co (the Sales Agents) under which we may sell an aggregate of up to 20 million shares of our common stock from time to time through the Sales Agents. To date we have issued approximately 7.0 million shares of our common stock in at the market offerings through the Sales Agents and raised net proceeds of approximately $8.8 million after deducting offering costs of approximately $331,000. As of December 31, 2010, we had debt outstanding of $34.9 million in principal, including $34.7 million in principal of our 2006 Notes maturing August 31, 2014 and $100,000 in principal of our 2005 Notes maturing February 20, 2025. The 2005 Notes are subject to redemption at the option of the holders or us beginning February 1, 2012.

Our cash, cash equivalents, and short-term investments at December 31, 2010 were $19.8 million, a decrease of $10.3 million from December 31, 2009. Based on our current plans and activities, we anticipate that our net cash burn (defined as cash used in operating activities plus capital expenditures and dividend payments) will be in the $16-$18 million range for the year ending December 31, 2011. In addition, we hope to generate royalties from our QS-21 product in the 2013-2014 timeframe.

We believe that, based on our current plans and activities, our working capital resources at December 31, 2010, anticipated revenues, and the estimated proceeds from our license, supply, and collaborative agreements will be sufficient to satisfy our liquidity requirements into 2012. We closely monitor our cash needs. We continue to monitor the likelihood of success of our key initiatives and are prepared to discontinue funding of such activities if they do not prove to be commercially feasible. In addition, we will continue to adjust other spending as needed in order to preserve liquidity. We expect to attempt to raise additional funds in advance of depleting our current funds. In order to fund our operations through 2011 and beyond, we will need to contain costs and raise additional funds. We may attempt to raise additional funds by: (1) licensing technologies or products to one or more collaborative partners, (2) renegotiating third party agreements, (3) completing an outright sale of selected assets, (4) securing additional debt financing, and/or (5) selling additional equity securities. Our ability to successfully enter into any such arrangements is uncertain, and if funds are not available, or not available on terms acceptable to us, we may be required to revise our planned clinical trials, other development activities, capital expenditures, and/or the scale of our operations. As noted above, we expect to attempt to raise additional funds in advance of depleting our current funds; however, we may not be able to

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raise funds or raise amounts sufficient to meet the long-term needs of the business. Satisfying long-term liquidity needs may require the successful commercialization of Oncophage and/or one or more partnering arrangements for our other Prophage Series vaccines, successful commercialization of vaccines containing QS-21 under development by our licensees, and potentially successful commercialization of other product candidates, each of which will require additional capital, as discussed above. Please see the Forward-Looking Statements section and the risks highlighted under Part I-Item 1A. Risk Factors of this Annual Report on Form 10-K.

Our future cash requirements include, but are not limited to, efforts to make Oncophage available in Russia and other jurisdictions we are currently exploring, as well as supporting our clinical trial and regulatory efforts and continuing our other research and development programs. Since inception, we have entered into various agreements with institutions and clinical research organizations to conduct and monitor our clinical studies. Under these agreements, subject to the enrollment of patients and performance by the applicable institution of certain services, we have estimated our payments to be $47.2 million over the term of the studies. Through December 31, 2010, we have expensed $46.5 million as research and development expenses and $46.3 million has been paid related to these clinical studies. The timing of expense recognition and future payments related to these agreements is subject to the enrollment of patients and performance by the applicable institution of certain services.

We have also entered into sponsored research agreements related to our product candidates that required payments of $6.5 million, all of which has been paid as of December 31, 2010. We plan to enter into additional sponsored research agreements, and we anticipate significant additional expenditures will be required to advance our clinical trials, apply for regulatory approvals, continue development of our technologies, and bring our product candidates to market. Part of our strategy is to develop and commercialize some of our product candidates by continuing our existing collaborative arrangements with academic and collaborative partners and licensees and by entering into new collaborations. As a result of our collaborative agreements, we will not completely control the efforts to attempt to bring those product candidates to market. We have various agreements, for example, with collaborative partners and/or licensees, which allow the use of our QS-21 adjuvant in numerous vaccines. These agreements grant exclusive worldwide rights in some fields of use and co-exclusive or non-exclusive rights in others. These agreements generally provide us with rights to manufacture and supply QS-21 to the collaborative partner or licensee and also call for royalties to be paid to us on future sales of licensed vaccines that include QS-21, which may or may not be achieved. Significant investment in manufacturing capacity could be required if we were to retain our manufacturing and supply rights.

Net cash used in operating activities for the year ended December 31, 2010 and 2009 was $14.8 million and $24.2 million, respectively. We continue to support and develop our QS-21 partnering collaborations, with the goal of generating royalties from this product in the 2013-2014 timeframe. Our future ability to generate cash from operations will depend on achieving regulatory approval of our product candidates, and market acceptance of Oncophage and our product candidates, achieving benchmarks as defined in existing collaborative agreements, and our ability to enter into new collaborations. Please see the Forward-Looking Statements section and the risks highlighted under Part I-Item 1A. Risk Factors of this Annual Report on Form 10-K.

The table below summarizes our contractual obligations as of December 31, 2010 (in thousands).

		Payments Due by Period			
	Total	Less than 1 Year	1 3 Years	3 5 Years	More than 5 Years
Long-term debt (1)	$ 46,542	$ 207	$ 103	$ 46,232	$
Operating leases	5,771	2,224	3,547		
Total	$ 52,313	$ 2,431	$ 3,650	$ 46,232	$

(1) Assumes the 2006 Notes are not converted and are paid in 2014. In certain circumstances, the 2006 Notes could be converted before then. Also includes fixed interest payments, some of which may be paid in kind, and assumes that the 2005 Notes are not converted and are paid on February 1, 2012. In certain

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circumstances, the 2005 Notes could be converted before then. In addition, the holders of the 2005 Notes can require us to purchase debt from them at certain dates between 2012 and 2020. If the 2005 Notes are not converted and we are not required to purchase the debt, the 2005 Notes mature on February 1, 2025. If the 2005 Notes were outstanding until maturity, there would be additional interest payments of $68,000 for the period 2012 through 2025.

Effective July 19, 2002, we sublet part of our Framingham facility to GTC Biotherapeutics, Inc. (GTC) and we leased related leasehold improvements and equipment under agreements that were to expire on December 31, 2006. GTC exercised its option to extend this lease until September 2010, the date our original lease expired. Under the terms of our original lease, we were obligated to pay our landlord approximately 7% of our rental income. Effective March 17, 2004, we sublet an additional part of our Framingham facility to PP Manufacturing, whose lease also expired in September 2010. Since September 30, 2010, we are no longer a party to any lease or subleasing arrangements for this facility. Effective July 30, 2010, we sublet part of our Lexington facility to Cubist Pharmaceuticals, Inc. whose lease expires in July 2012. Our Lexington facility and New York office leases expire August 2013 and April 2012, respectively.

We are currently involved in certain legal proceedings as detailed in Item 3 above and Note 16 of the notes to our consolidated financial statements. While we currently believe that the ultimate outcome of any of these proceedings will not have a material adverse effect on our financial position, results of operations, or liquidity, litigation is subject to inherent uncertainty. Furthermore, litigation consumes both cash and management attention.

Inflation

We believe that inflation has not had a material adverse effect on our business, results of operations, or financial condition to date.

Related Parties

In March 1995, we entered into a consulting agreement with Dr. Pramod Srivastava, our scientific founder and a former member of our Board of Directors, and upon its expiration in March 2006, we entered into a new consul