ANTIGENICS INC /DE/
Form S-3/A
June 10, 2005

Table of Contents

As filed with the Securities and Exchange Commission on June 10, 2005
Registration No. 333-125197

UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Pre-effective Amendment No. 1
to
Form S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Antigenics Inc.
(Exact name of registrant as specified in its charter)

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

630 Fifth Avenue, Suite 2100
New York, New York 10111
(212) 994-8200
(Address, including zip code, and telephone number, including area code of principal executive offices)

Garo H. Armen
Chief Executive Officer
Antigenics Inc.
630 Fifth Avenue, Suite 2100
New York, New York 10111
(212) 994-8200
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Please send copies of all communications to:
Paul Kinsella
Ropes & Gray LLP
One International Place
Boston, Massachusetts 02110
(617) 951-7000

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement.

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

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

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

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

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box: o

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until this Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

Table of Contents

The information in this prospectus is not complete and may be changed. These securities may not be sold in a public offering until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, JUNE 10, 2005

PROSPECTUS

Antigenics Inc.
$50,000,000 Principal Amount of 5.25% Convertible Senior Notes Due 2025 and 4,645,115 Shares of Antigenics Common Stock Issuable on Conversion of the Notes

We issued the notes in a private placement in January 2005. This prospectus may be used by selling securityholders to resell from time to time their notes and the shares of common stock issuable upon conversion of their notes. We will not receive any of the proceeds from the resale of the notes or the shares issuable upon conversion of the notes.

The notes accrue interest at an annual rate of 5.25%. Interest on the notes is due on February 1 and August 1 of each year. The first interest payment will be made on August 1, 2005. The notes will mature on February 1, 2025.

Holders may convert their notes at any time prior to stated maturity. The initial conversion rate, which is subject to adjustment, is 92.9023 shares per $1,000 principal amount of notes. This represents an initial conversion price of approximately $10.76 per share.

A holder that surrenders notes for conversion in connection with certain fundamental changes that occur before February 1, 2012 may in certain circumstances be entitled to an increase in the conversion rate. However, in lieu of increasing the conversion rate applicable to those notes, we may in certain circumstances elect to change our conversion obligation so that the notes will be convertible into shares of an acquiring company s common stock.

On or after February 1, 2012, we may from time to time at our option redeem the notes, in whole or in part, for cash, at a redemption price equal to 100% of the principal amount of the notes we redeem, plus any accrued and unpaid interest to, but excluding, the redemption date. We must make at least 14 semi-annual interest payments on the notes before we may redeem them.

On each of February 1, 2012, February 1, 2015 and February 1, 2020, holders may require us to purchase all or a portion of their notes at a purchase price in cash equal to 100% of the principal amount of the notes to be purchased, plus any accrued and unpaid interest to, but excluding, the purchase date. Holders may require us to repurchase all or a portion of their notes upon a fundamental change, as described in this prospectus, at a repurchase price, in cash, equal to 100% of the principal amount of the notes to be repurchased, plus any accrued and unpaid interest to, but excluding, the fundamental change repurchase date.

The notes are our senior unsecured obligations and rank equally with all of our existing and future senior unsecured indebtedness. The notes are effectively subordinated to all of our existing and future secured indebtedness and all existing and future liabilities of our subsidiaries, including trade payables. As of March 31, 2005, we had approximately $8.4 million of outstanding secured indebtedness, and our subsidiaries had total liabilities, excluding intercompany liabilities, of $3.1 million. All of this indebtedness effectively ranks senior to the notes.

The notes have been designated for trading in The PORTAL[sm] Market, a subsidiary of The NASDAQ Stock Market, Inc. Any notes that are resold by means of this prospectus will no longer be eligible for trading in The PORTAL[sm] Market. Our common stock is listed on the NASDAQ National Market under the symbol AGEN. On June 9, 2005, the last reported sale price of our common stock was $6.22 per share.

Investing in the notes and shares of our common stock involves a high degree of risk. You should carefully read and consider the Risk Factors beginning on page 7.

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

The date of this prospectus is , 2005

TABLE OF CONTENTS

You should rely only on the information contained or incorporated by reference in this prospectus. We have not, nor have any of the selling securityholders, authorized anyone to provide you with different information. The information contained in this prospectus is correct only as of the date hereof, regardless of the time of the delivery of this prospectus or any sale of the securities described in this prospectus. The selling securityholders are not making an offer to sell nor are they seeking an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Table of Contents

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and the documents incorporated into it by reference. Because this is a summary, it does not contain all of the information that you should consider before investing in our securities. You should read the entire prospectus and the documents incorporated by reference carefully, including the section entitled Risk factors.

Unless we indicate otherwise in this prospectus, Antigenics, we, us and our refer to Antigenics Inc. and its subsidiaries. The notes are obligations of Antigenics Inc. and not any of its subsidiaries. Accordingly, in descriptions of the notes and obligations under the indenture Antigenics , we , us and our refer to Antigenics Inc. alone.

ANTIGENICS INC.

We are a biotechnology company developing technology and products to treat cancers, infectious diseases and autoimmune disorders, primarily based on immunological approaches. Our most advanced product candidate is Oncophage®, a personalized therapeutic cancer vaccine being tested in several types of cancer, including in Phase 3 clinical trials for the treatment of renal cell carcinoma, the most common type of kidney cancer, and metastatic melanoma. Our product candidate portfolio also includes (1) AG-858, a personalized therapeutic cancer vaccine in a Phase 2 clinical trial for the treatment of chronic myelogenous leukemia, (2) AG-702/ AG-707, a therapeutic vaccine program in Phase 1 clinical development for the treatment of genital herpes, and (3) Aroplatin™, a liposomal chemotherapeutic currently completing pre-clinical reformulation and testing. Our related business activities include research and development, regulatory and clinical affairs, clinical manufacturing, business development, marketing and administrative functions that support these activities.

OUR PRODUCTS UNDER DEVELOPMENT

Introduction

Heat shock proteins, our founding technology platform, form the basis for our most advanced product candidate, Oncophage, and for our AG-858 and AG-702/ AG-707 product candidates. We have observed clinical activity in Phase 1, Phase 1/2 and Phase 2 trials of Oncophage in terms of improvement or stabilization of disease in multiple cancer types. This includes data demonstrating complete disappearance (a complete response) or substantial shrinkage (a partial response) of tumor lesions in a portion of patients with renal cell carcinoma, melanoma and lymphoma. Additionally, in a portion of patients who were rendered disease-free by surgery, we have observed signs of positive impact on disease such as disease-free survival in resectable pancreatic cancer and increased survival in a subset population in stage IV colon cancer. In our studies to date, the vaccine has shown that it may have a favorable safety profile. The most common side effects have been mild to moderate injection site reactions and transient low-grade fevers. We believe that this human data further supports the broad applicability and corresponding commercial potential of our heat shock protein candidates.

Oncophage is a personalized therapeutic cancer vaccine that is based on a heat shock protein called gp96, and it is currently in Phase 3 clinical trials for renal cell carcinoma and metastatic melanoma. Oncophage has received Fast Track designation and Orphan Drug designation from the US Food and Drug Administration, also known as the FDA, for both renal cell carcinoma and metastatic melanoma.

AG-858 is a personalized therapeutic cancer vaccine based on a different heat shock protein called HSP70, which is being tested in combination with Gleevec™ (imatinib mesylate, Novartis) in a Phase 2 clinical trial for the treatment of chronic myelogenous leukemia, a cancer of the blood system in which too many white blood cells are produced in the bone marrow.

AG-702/AG-707 is our therapeutic vaccine program for the treatment of genital herpes. While AG-702 consists of a heat shock protein (Hsc70) associated with a single synthetic peptide from the herpes simplex virus-2, AG-707 is a multivalent vaccine (a type of vaccine that addresses multiple components of the virus) that contains multiple herpes simplex virus-2 homologous peptides. We initiated

1

Table of Contents

a proof-of-principle Phase 1 trial for AG-702 in the fourth quarter of 2001. We plan to file an investigational new drug application (IND) during the first half of 2005 for AG-707, and we plan to initiate a Phase 1 clinical trial of AG-707 shortly thereafter. We have experienced delays in the animal experiments performed to support the basis of clinical development and an IND filing. We continue to work towards achieving an effective formulation from our animal studies and expect to complete these studies in the first half of 2005. We do not anticipate further developing AG-702 given that AG-707 should be beneficial to a larger number of patients with genital herpes.

Our other product candidates and clinical programs include Aroplatin, a novel liposomal third-generation platinum chemotherapeutic that has been studied in two trials, a Phase 2 trial of patients with colorectal cancer and a Phase 1 trial of patients with other solid tumors. Platinum chemotherapeutics are cancer drugs containing the metallic element platinum, which has been shown to have some anti-cancer effects. In the case of Aroplatin, the active platinum drug component is encapsulated in a liposome, which is a spherical particle of phospholipids that are components of human cell membranes. Our technologies also include QS-21, an adjuvant, or companion compound, studied in both therapeutic and prophylactic vaccines to improve the quality of immune response.

Through our preclinical research programs, we intend to develop additional novel compounds to treat cancer and infectious diseases that are designed to be more efficacious and safer than conventional therapies. Our lead preclinical program is focused on a next-generation Oncophage vaccine, which incorporates several important innovations. With these advances, we expect to be able to manufacture sufficient quantities of a personalized cancer vaccine for patient treatment from much smaller tumor tissue samples. We are also studying pathways through which heat shock proteins activate the immune system and plan on initiating combination therapy studies with Oncophage and other immunomodulators and chemotherapeutics during 2005.

Heat Shock Protein Technology

Heat shock proteins, also known as HSPs, are also called stress proteins. HSPs are a group of proteins that are induced when a cell undergoes various types of environmental stresses like heat, 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, heat shock proteins play a major role in transporting fragments of proteins called peptides, including antigenic peptides, within a cell, and are thus called chaperones. Antigenic peptides are those portions of a protein that stimulate immune response when recognized by the immune system. Because HSPs chaperone peptides within the cell, they bind a broad array of antigenic peptides and facilitate their recognition by the immune system. Thus, HSPs help present the antigenic fingerprint of the cell to the immune system.

Although heat shock proteins are normally found inside cells, they also serve an important purpose when found extracellularly, meaning outside of cells. When they are found outside of cells, it indicates that a cell has undergone necrosis, a type of rupturing cell death caused by disease, mutation or injury whereby a cell s contents are spilled into the body tissue. Extracellular HSPs are a powerful danger signal to the immune system and they therefore are capable of generating a targeted immune response against the infection or disease responsible for the necrotic cell death.

Combined, the intracellular and extracellular functions of heat shock proteins form the basis of our technology. The chaperoning nature of heat shock proteins allows us to produce vaccines containing the antigenic peptides of a given disease. In the case of cancer, the vaccines are personalized, consisting of heat shock proteins purified from a patient s tumor cells which remain bound, or complexed, to a broad array of peptides produced by that patient s tumor. These heat shock protein-peptide complexes, also known as HSPPCs, when injected into the skin, have the ability to stimulate a powerful T-cell-based immune response 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, we believe that a personalized vaccination approach is required to generate a more robust and targeted immune response.

Table of Contents

For diseases that are not highly variable from one patient to another, such as genital herpes, we do not believe that a personalized vaccination approach is required. For example, in our AG-702/ AG-707 program for the treatment of genital herpes, we complex, or bind, one or several defined antigenic herpes peptides to a heat shock protein (Hsc70) that we genetically engineer, creating an HSPPC. This HSPPC, when injected into the skin, is designed to elicit a T-cell-based immune response to the synthetic peptides carried by the heat shock protein.

PRODUCT DEVELOPMENT PORTFOLIO

Below is the clinical status of our lead product candidates under development.

	Status		
Product	**Phase 3(1)**	**Phase 2**	**Phase 1**
Oncophage	Renal cell carcinoma(3) Melanoma(2)	Colorectal cancer(2) Non-Hodgkin s lymphoma(2) Gastric cancer(2) Metastatic renal cell carcinoma Lung cancer	Pancreatic cancer(2)
AG-858		Chronic myelogenous leukemia	
AG-702			Genital herpes
Aroplatin		Colorectal cancer(2)	Solid tumors

(1) These trials are multi-center trials being conducted in the US as well as internationally.

(2) These trials are closed to enrollment.

(3) Part I of this trial is closed to enrollment. Part II of this trial is open to enrollment.

OUR CORPORATE INFORMATION

Antigenics L.L.C. was formed as a Delaware limited liability company in 1994 and converted to Antigenics Inc., a Delaware corporation, in February 2000. Our principal executive offices are located at 630 Fifth Avenue, Suite 2100, New York, NY 10111, and our main telephone number is (212) 994-8200. You can find additional information about us in our filings with the SEC. See Where you can find additional information.

Table of Contents

THE NOTES

The following is a brief summary of the terms of the notes. For a more complete description of the notes, see Description of notes in this prospectus.

Notes	$50,000,000 aggregate principal amount of 5.25% convertible senior notes due February 1, 2025.
Maturity	The notes will mature on February 1, 2025, unless earlier redeemed, repurchased or converted.
Interest payment dates	The notes accrue interest at 5.25% per annum on the principal amount of the notes, payable semi-annually in arrears on February 1 and August 1 of each year, starting on August 1, 2005, to holders of record at the close of business on the preceding January 15 and July 15, respectively. Interest accrues on the notes from and including January 25, 2005 or from and including the last date in respect of which interest has been paid or provided for, as the case may be, to, but excluding, the next interest payment date or maturity date, as the case may be.
Ranking	The notes are our senior unsecured obligations and rank equally with all of our existing and future senior unsecured indebtedness. The notes are effectively subordinated to all of our existing and future secured indebtedness and all existing and future liabilities of our subsidiaries, including trade payables. As of March 31, 2005, we had approximately $8.4 million of outstanding secured indebtedness, and our subsidiaries had total liabilities, excluding intercompany liabilities, of $3.1 million. All of this indebtedness effectively ranks senior to the notes. See Description of notes Ranking.
Conversion rights	Holders may convert their notes at any time prior to stated maturity. The initial conversion rate, which is subject to adjustment, is 92.9023 shares per $1,000 principal amount of notes. This represents an initial conversion price of approximately $10.76 per share. A holder that surrenders notes for conversion in connection with certain fundamental changes that occur before February 1, 2012 may in certain circumstances be entitled to an increase in the conversion rate. The amount of the increase in the conversion rate, or number of additional shares issuable upon conversion, if any, will be based on the price paid per share of our common stock in the transaction, which we refer to as the applicable price, and the effective date of the fundamental change. A description of how the number of additional shares will be calculated and a table showing the number of additional shares that would apply at various applicable prices and fundamental change effective dates, based on assumed interest and conversion rates, are set forth under Description of notes Conversion rights. If the actual applicable price is less than $8.97 per share (subject to adjustment) or greater than $52.50 per share (subject to adjustment), we will not increase the conversion rate. However, in lieu of increasing the conversion rate applicable to those notes, we may in certain circumstances elect to change our

Table of Contents

	conversion obligation so that the notes will be convertible into shares of an acquiring company s common stock. See Description of notes Conversion rights.
Sinking fund	None.
Redemption of notes at our option	On or after February 1, 2012, we may from time to time at our option redeem the notes, in whole or in part, at a redemption price in cash equal to 100% of the principal amount of the notes we redeem, plus any accrued and unpaid interest to, but excluding, the redemption date. See Description of notes Redemption of notes at our option.
Purchase of notes by us at the option of the holder	On each of February 1, 2012, February 1, 2015 and February 1, 2020, holders may require us to purchase all or a portion of their notes at a purchase price in cash equal to 100% of the principal amount of the notes to be purchased, plus any accrued and unpaid interest to, but excluding, the purchase date. See Description of notes Purchase of notes by us at the option of the holder.
Right of holder to require us to repurchase notes if a repurchase event occurs	If a fundamental change, as described in this prospectus, occurs, holders may require us to repurchase all or a portion of their notes for cash at a repurchase price equal to 100% of the principal amount of the notes to be repurchased, plus any accrued and unpaid interest to, but excluding, the repurchase date. See Description of notes Holders may require us to repurchase their notes upon a fundamental change.
Events of default	If an event of default on the notes has occurred and is continuing, the principal amount of the notes plus any premium and accrued and unpaid interest may become immediately due and payable. These amounts automatically become due and payable upon certain events of default. See Description of notes Events of default.
Use of proceeds	We will not receive any proceeds from the sale of the notes or the shares of common stock issuable upon conversion of the notes.
DTC eligibility	The notes were issued in book-entry-only form and are represented by one or more global securities, without interest coupons, deposited with, or on behalf of, DTC and registered in the name of a nominee of DTC. Beneficial interests in the notes are shown on, and transfers are effected only through, records maintained by DTC and its direct and indirect participants. Except in limited circumstances, holders may not exchange interests in their notes for certificated securities. See Description of notes Form, denomination and registration of notes.
Listing and trading	The notes are not listed on any securities exchange or included in any automated quotation system. Any notes that are sold by means of this prospectus will no longer be eligible for trading in

Table of Contents

	The PORTAL[sm] Market. Our common stock is quoted on the NASDAQ National Market under the symbol AGEN.
Material US federal tax considerations	For a discussion of certain US federal tax considerations relating to the purchase, ownership and disposition of the notes and shares of common stock into which the notes are convertible, see Material US federal tax considerations.
Risk factors	In analyzing an investment in the notes offered by this prospectus, prospective investors should carefully consider, along with other matters referred to in this prospectus, the information set forth under Risk factors.

Table of Contents

RISK FACTORS

Investing in the notes involves a high degree of risk. In addition to the other information included and incorporated by reference in this prospectus, you should carefully consider the risks described below before purchasing the notes. If any of the following risks actually occurs, our business, results of operations and financial condition will likely suffer. As a result, the trading price of the notes and our common stock may decline, and you might lose part or all of your investment.

RISKS RELATED TO OUR BUSINESS

If we incur operating losses for longer than we expect, we may be unable to continue our operations.

From our inception through March 31, 2005, we have generated net losses totaling approximately $354 million. Our net losses for the three months ended March 31, 2005, and for the years ended December 31, 2004, 2003, and 2002, were approximately $18.0 million, $56.2 million, $65.9 million, and $55.9 million, respectively. We expect to incur significant losses over the next several years as we continue our clinical trials, apply for regulatory approvals, continue development of our technologies, and expand our operations. Phase 3 clinical trials are particularly expensive to conduct, and in February 2005 we initiated part II of our Phase 3 clinical trial in renal cell carcinoma. Furthermore, our ability to generate cash from operations is dependent on if and when we will be able to commercialize our product candidates. If we incur operating losses for longer than we expect, we may be unable to continue our operations.

If we fail to obtain the capital necessary to fund our operations, we will be unable to advance our development programs and complete our clinical trials.

On March 31, 2005, we had approximately $114.1 million in cash, cash equivalents and short-term investments. With our current working capital we expect that we could fund our development programs, clinical trials, and other operating expenses into 2006. We plan to raise additional funds prior to that time. For the three months ended March 31, 2005, the sum of our average monthly cash used in operating activities plus our average monthly capital expenditures was approximately $6.7 million. Total capital expenditures for the three months ended March 31, 2005 were $1.1 million and we anticipate capital expenditures of up to $2.0 million during the remainder of 2005. Since our inception, we have financed our operations primarily through the sale of equity. In order to finance our future operations, we will be required to raise additional funds in the capital markets, through arrangements with corporate partners, or from other sources. Additional financing, however, 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 programs and some or all of our clinical trials, including the development programs and clinical trials supporting our most advanced product candidate, Oncophage. We also may be forced to license technologies to others under agreements that allocate to third parties substantial portions of the potential value of these technologies.

We have significant long-term debt and we may not be able to make interest or principal payments when due.

As of March 31, 2005, our total long-term debt, excluding the current portion, was approximately $53 million. The 5.25% convertible senior notes due 2025 do not restrict our ability or the ability of our subsidiaries to incur additional indebtedness, including debt that effectively ranks senior to the notes. On each of February 1, 2012, February 1, 2015 and February 1, 2020, holders may require us to purchase their notes for cash equal to 100% of the principal amount of the notes, plus any accrued and unpaid interest. Holders may also require us to repurchase their notes upon a fundamental change, as defined, at a repurchase price, in cash, equal to 100% of the principal amount of the notes to be repurchased, plus any accrued and unpaid interest. 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. To date, we have had negative cash flow from operations. For the three months ended March 31, 2005, and for the year ended December 31, 2004, net cash used in operating activities

Table of Contents

was approximately $19 million and $60 million, respectively. Assuming no additional interest-bearing debt is incurred and none of the notes are converted, redeemed, repurchased or exchanged before February 1, 2012, our debt service requirements (payments of principal and interest) are $6.5 million during 2005, $7.2 million during 2006, $2.7 million during 2007 and $2.6 million annually during 2008 and thereafter until the notes are no longer outstanding. Unless we are able to generate sufficient operating cash flow to service our outstanding debt, we will be required to raise additional funds or default on our obligations, including our obligations under the notes.

Because the FDA has told to us that part I of our current Phase 3 trial in renal cell carcinoma, by itself, will not be sufficient to support a biologics license application for product approval, unless the FDA changes its position, we would not expect to generate product revenue from sales of Oncophage for at least several years, if ever.

On September 3, 2003, the FDA placed our Phase 3 Oncophage clinical trials in renal cell carcinoma and in melanoma on partial clinical hold. The FDA s written correspondence instituting the partial clinical hold indicated that Oncophage was not sufficiently characterized. On October 22, 2003, we submitted to the FDA additional specifications for purity, identity, potency and pH, which represent product characterization data, and on November 23, 2003, the FDA lifted the partial clinical hold. Even though the FDA lifted the partial clinical hold, the FDA has informed us that, for purposes of part I of our Phase 3 trial in renal cell carcinoma and our Phase 3 trial in melanoma, Oncophage has been insufficiently characterized and that the results obtained with an insufficiently characterized product could not be used to provide efficacy data in support of a biologics license application, or BLA. The FDA deemed the Oncophage provided to patients before December 2003 to be insufficiently characterized because it had not undergone the full battery of tests required for drugs used in pivotal trials. Some of these tests, such as potency assays, were not fully developed until after September 2003. The imposition of the partial clinical hold prevented us from enrolling new patients in our Phase 3 clinical trials between September 3, 2003 and November 21, 2003. We believe that we addressed the comments the FDA raised in connection with the partial clinical hold. After the clinical hold was lifted, the FDA asked us to implement the use of the qualified potency assays to release vaccine lots for all trials of Oncophage, including our Phase 3 trials. After the clinical hold was lifted, we submitted, during 2004, our validation package to the FDA for the qualified potency assays, and in May 2005 we successfully concluded discussions with the FDA. Validation of the assays refers, in general terms, to establishing the robustness and reproducibility of the assays on an ongoing basis and under various different conditions to demonstrate that the qualified potency assays, accepted by the FDA for continuation of the clinical trial, work consistently. The validated potency assays have been used to test product administered since December 2003, and we have commenced tests on frozen stored portions of product administered to patients prior to December 2003. We believe we have addressed all product characterization issues raised by the FDA to date other than the retrospective potency testing of Oncophage product administered to patients before December 2003.

Because the FDA has indicated that, by itself, part I of our ongoing Phase 3 clinical trial in renal cell carcinoma is not sufficient to support a BLA filing, we have expanded our clinical development plan by initiating a part II to this Phase 3 trial in a similar patient population. The FDA has agreed with this registration plan, which comprises two components part I and part II. The FDA has told us that part I alone will not be sufficient for approval, as they consider part II of the trial as potentially providing the definitive evidence of safety and efficacy; however, we expect that part I will be accepted as part of the BLA filing. While the FDA has expressly excluded the possibility that part I of our renal cell carcinoma trial alone can support a BLA filing, we intend to complete part I, which is a large, controlled study, perform final analysis, and review the data closely. Should the results from the first part of the trial be clearly positive in terms of clinical outcomes, we plan to submit the data to the FDA and request that the agency reconsider its position regarding the use of the data from part I of the trial alone to support a BLA filing. We expect to support that position with data that may demonstrate that Oncophage used in part I of the study should be considered sufficiently characterized. We would expect to derive that data from the additional tests we plan to perform on frozen stored portions of the product administered to patients prior to December 2003. We have commenced these additional tests and plan to have them completed in time

Table of Contents

for any BLA filing. We believe that the FDA is unlikely to reverse its position unless part I of the trial demonstrates significant benefit to patients. We believe that demonstration of efficacy might be persuasive because (1) part I of our Phase 3 renal cell carcinoma trial is designed to show that patients being treated with Oncophage have a statistically significant benefit in terms of recurrence-free survival over patients in the observation arm, (2) Oncophage appears to have a favorable safety profile, particularly when compared with the toxicity associated with many cancer drugs, (3) part I of the trial represents the largest single randomized trial to date in this patient population and was designed to show statistically significant results, and (4) the patients with the stage of renal cell carcinoma addressed in this trial have no approved post-surgical treatment options. Other companies have submitted BLAs, and obtained approvals, based on data from non-definitive Phase 2 and Phase 3 studies while they complete confirmatory studies. We are not aware of a situation, however, in which the FDA has reconsidered its position that a clinical trial could not be considered pivotal, and therefore would not support licensure, because of its determination that the product candidate was insufficiently characterized. However, as noted previously, we plan to perform additional tests of frozen stored Oncophage product samples produced prior to December 2003 and attempt to demonstrate that our product candidate should be considered sufficiently characterized. There is no assurance that we will be successful in demonstrating that our product candidate is sufficiently characterized or that the FDA would accept such a strategy. The FDA usually requires prospective, rather than retrospective, testing.

Even if we are able to demonstrate that the Oncophage used in part I of the trial should be considered sufficiently characterized and part I of the trial demonstrates significant benefit to patients, the FDA may continue to adhere to its current position that the data from this part of the trial cannot, by itself, support a BLA filing. In addition, the results of our two potency tests may not indicate that the Oncophage used in part I of the trial is sufficiently characterized. Furthermore, part I may not meet its statistical endpoint, or the FDA could determine that making Oncophage available based on the part I results is not in the best interests of patients. We estimate that completing part II of the study will take at least three years and cost between $20 million and $40 million. Furthermore, we intend to continue with part II of the renal cell carcinoma study unless and until the FDA indicates that it is not necessary.

We may not be able to secure additional financing to complete part II of the renal cell carcinoma trial even if the results from part I of the trial are positive. If we cannot raise funding because we are unable to convince the FDA that the data from part I should be deemed sufficient, by itself, to support a BLA filing, we may become insolvent.

Because we expect to conduct additional Phase 3 clinical trials of Oncophage in the treatment of melanoma prior to submitting a BLA for this indication, we will not commercialize Oncophage in this indication for several years, if ever.

We have concluded enrollment in our Phase 3 trial of Oncophage in patients with metastatic melanoma. We believe that, due to a relatively high failure rate in vaccine manufacturing, this study will not, by itself, support a BLA filing. Even if we had not experienced the high manufacturing failure rate, the FDA has indicated that this study, like part I of our Phase 3 renal cell carcinoma study, could not, by itself, support a BLA filing because the FDA views the Oncophage administered to patients in this study prior to December 2003 as insufficiently characterized. We have not yet had any specific discussions with the FDA regarding our clinical development plan for melanoma. Accordingly, we do not know the types of studies that the FDA will require to support a BLA filing. Even if the FDA were to indicate agreement with our clinical development plan, that plan may fail to support a BLA filing for many reasons, including failure of the trials to demonstrate that Oncophage is safe and effective in this indication, failure to conduct the studies in compliance with the clinical trial protocols, or a change in the FDA s views.

Our commercial launch of Oncophage may be delayed or prevented, which would diminish our business prospects.

In December 2003, we announced that the Data Monitoring Committee, or DMC, had convened as scheduled for the interim analysis of part I of our Phase 3 clinical trial of Oncophage in the treatment of

Table of Contents

renal cell carcinoma, C-100-12. The DMC is a panel of cancer specialists who review the safety and conduct of the trial at regular intervals but are not otherwise involved in the study. The DMC has no direct relationship with the FDA but can make recommendations regarding the further conduct of the trial, which recommendations are reported to the FDA. The use of the DMC is intended to enhance patient safety and trial conduct. The DMC recommended that the trial proceed as planned and did not require that we change the number of patients required to meet the trial s objectives. Part I of our Phase 3 renal cell carcinoma trial is designed with the intent to show that patients in the Oncophage arm demonstrate a statistically significant benefit in recurrence-free survival over the patients in the observation arm. We interpreted the recommendation by the DMC that we would not need to add patients in order to potentially achieve a statistically significant benefit as an encouraging development, indicating that the trial could demonstrate efficacy goals without increasing the number of patients in the trial. The DMC s recommendations do not assure either that the trial will demonstrate statistically significant results or that the trial will prove adequate to support approval of Oncophage for commercialization in the treatment of patients with renal cell carcinoma. The assessment of the interim analysis by the DMC is preliminary. The final data from the trial may not demonstrate efficacy and safety. Furthermore, data from clinical trials are subject to varying interpretations.

Inconclusive or negative final data from part I of our Phase 3 renal cell carcinoma trial would have a significant negative impact on our prospects. If the results in any of our clinical trials are not positive, we may abandon development of Oncophage for the applicable indication.

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

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. Our most advanced product candidate, Oncophage, is a novel therapeutic cancer vaccine that is personalized for each patient. To date, the FDA has not approved any therapeutic cancer vaccines for commercial sale, and foreign regulatory agencies have approved only a limited number. Both the FDA and foreign regulatory agencies, including the European Medicines Agency responsible for product approvals in Europe, have relatively little experience in reviewing personalized oncology therapies, and the partial clinical hold that the FDA had placed, and subsequently lifted, on our current Phase 3 Oncophage clinical trials primarily related to product characterization issues partially associated with the personalized nature of Oncophage. Oncophage may experience a long regulatory review process and high development costs, either of which could delay or prevent our commercialization efforts. We also initiated communications with health regulatory authorities in other jurisdictions to discuss requirements for the approval of Oncophage in renal cell carcinoma. As of March 31, 2005, we have spent approximately 10 years and $176 million on our research and development program in heat shock proteins for cancer.

To obtain regulatory approvals, we must, among other requirements, complete carefully controlled and well-designed clinical trials demonstrating that a particular product candidate is safe and effective for the applicable disease. Several biotechnology companies have failed to obtain regulatory approvals because regulatory agencies were not satisfied with the structure or conduct of clinical trials or the ability to interpret the data from the trials; similar problems could delay or prevent us from obtaining approvals. We initiated part II of our Phase 3 trial for Oncophage in renal cell carcinoma in early 2005. Even after reviewing our protocols for these trials, the FDA and other regulatory agencies may not consider the trials to be adequate for registration and may disagree with our overall strategy to seek approval for Oncophage in renal cell carcinoma. In this event, the potential commercial launch of Oncophage would be at risk, which would likely have a materially negative impact on our ability to generate revenue and our ability to secure additional funding.

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. Because we rely on third-party clinical investigators and contract research organizations to conduct our clinical trials, we may encounter delays outside our control, particularly if our relationships with any third-party clinical investigators or contract

Table of Contents

research organizations are adversarial. The timing and success of our Phase 3 trials, in particular, are also dependent on the FDA and other regulatory agencies accepting each trial s protocol, statistical analysis plan, product characterization tests, and clinical data. If we are unable to satisfy the FDA and other regulatory agencies with such matters, including the specific matters noted above, or our Phase 3 trials yield inconclusive or negative results, we will be required to modify or expand the scope of our Phase 3 studies or conduct additional Phase 3 studies to support BLA filings, including additional studies beyond the new part II Phase 3 trial in renal cell carcinoma and additional Phase 3 trials in melanoma. In addition, the FDA may request additional information or data that is not readily available. Delays in our ability to respond to such an FDA request would delay, and failure to adequately address all FDA concerns would prevent, our commercialization efforts.

In addition, we, or the FDA, might further delay or halt our clinical trials for various reasons, including but not limited to:

- we may fail to comply with extensive FDA regulations;
- a product candidate may not appear to be more effective than current therapies;
- a product candidate may have unforeseen or significant adverse side effects or other safety issues;
- the time required to determine whether a product candidate is effective may be longer than expected;
- we may be unable to adequately follow or evaluate patients after treatment with a product candidate;
- patients may die during a clinical trial because their disease is too advanced or because they experience medical problems that may not be related to the product candidate;
- sufficient numbers of patients may not enroll in our clinical trials; or
- we may be unable to produce sufficient quantities of a product candidate to complete the trial.

Furthermore, regulatory authorities, including the FDA, may have varying interpretations of our pre-clinical and clinical trial data, which could delay, limit, or prevent regulatory approval or clearance. Any delays or difficulties in obtaining regulatory approvals or clearances for our product candidates may:

- adversely affect the marketing of any products we or our collaborators develop;
- impose significant additional costs on us or our collaborators;
- diminish any competitive advantages that we or our collaborators may attain; and
- limit our ability to receive royalties and generate revenue and profits.

If we do not receive regulatory approval for our product candidates in a timely manner, we will not be able to commercialize them in the timeframe anticipated, and, therefore, our business will suffer.

We must receive separate regulatory approvals for each of our product candidates for each type of disease indication before we can market and sell them in the United States or internationally.

We and our collaborators cannot sell any drug or vaccine until we receive regulatory approval from governmental authorities in the United States, and from similar agencies in other jurisdictions. Oncophage and any other drug candidate could take a significantly longer time to gain regulatory approval than we expect or may never gain approval or may gain approval for only limited indications.

Table of Contents

Even if we do receive regulatory approval for our product candidates, the FDA or international regulatory authorities will impose limitations on the indicated uses for which our products may be marketed or subsequently withdraw approval, or take other actions against us or our products adverse to our business.

The FDA and international 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, may be withdrawn if problems occur after initial marketing. Failure to comply with applicable FDA and other 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 and criminal prosecution.

Delays enrolling patients and/or the timing of clinical events in our studies will slow or prevent completion of clinical trials.

We have encountered in the past, and may encounter in the future, delays in initiating trial sites and in enrolling patients into our clinical trials. Future enrollment delays will postpone the dates by which we expect to complete the impacted trials and the potential receipt of regulatory approvals. If we fail to enroll sufficient numbers of patients in clinical trials, the trials may fail to demonstrate the efficacy of a product candidate at a statistically significant level. While such trials may help support our efforts to obtain marketing approval, they generally would not, by themselves, be sufficient for obtaining approval. In our cancer trials, enrollment difficulties may arise due to many factors, including the novel nature of Oncophage, the identification of patients meeting the specific criteria for inclusion in our trials, the speed by which participating clinical trial sites review our protocol and allow enrollment, and any delay in contract negotiations between us and the participating clinical trial sites. In addition, we may encounter problems in our clinical trials due to the advanced disease state of the target patient population. Even if our patient enrollment is adequate, patients may die during a clinical trial if their disease is too advanced or because they experience problems that may be unrelated to the product candidate. A high dropout rate in a trial may undermine the ability to gain statistically significant data from the study.

Part I and part II of our Phase 3 study trials in renal cell carcinoma are event driven trials. Therefore, final analysis of the trials will be triggered once a specified number of events occur. An event is defined as a recurrence of a patient s renal cell carcinoma or death of a patient. We currently anticipate that the earliest the final event will occur to trigger final analysis of our part I renal cell carcinoma trial is during the third quarter of 2005. We continue to adjust this estimate of the timing based on our monitoring of the number of events. While this time estimate is based on our current expectations, we do not control the timing of occurrence of events in the trial, and there can be no assurance that the total number of required events will occur when predicted.

If new data from our research and development activities continues to modify our strategy, then we expect to continually adjust our projections of timelines and costs of programs; this uncertainty may depress the market price of our stock and increase our expenses.

Because we are focused on novel technologies, our research and development activities, including our 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 are sometimes a daily occurrence 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. These issues are pronounced in our efforts to commercialize Oncophage, which represents an unprecedented approach to the treatment of cancer.

Table of Contents

Failure to enter into significant collaboration agreements may hinder our efforts to commercialize Oncophage and will increase our need to rely on equity sales to fund our operations.

We are engaged in efforts to partner Oncophage, our most advanced product candidate, with a pharmaceutical or larger biotech company to assist us with global commercialization. While we have been pursuing these business development efforts for several years, we have not negotiated a definitive agreement relating to the potential commercialization of Oncophage. Many larger companies may be unwilling to commit to a substantial agreement prior to receipt of additional clinical data or, in the absence of such data, may demand economic terms that are unfavorable to us. Even if Oncophage generates favorable clinical data, we may not be able to negotiate a transaction that provides us with favorable economic terms. While some other biotechnology companies have negotiated large collaborations, we may not be able to negotiate any agreements with terms that replicate the terms negotiated by those other companies. We may not, for example, obtain significant upfront payments or substantial royalty rates. Some larger companies are skeptical of the commercial potential and profitability of a personalized product candidate like Oncophage. If we fail to enter into such collaboration agreements, our efforts to commercialize Oncophage may be undermined. In addition, if we do not raise funds through collaboration agreements, we will need to rely on sales of additional securities to fund our operations. Sales of additional equity may substantially dilute the ownership of existing stockholders.

We may not receive significant payments from collaborators due to unsuccessful results in existing collaborations or failure to enter into future collaborations.

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 and preclinical and clinical testing. Our collaborations involving QS-21, for example, depend on our licensees successfully completing clinical trials and obtaining regulatory approvals. These activities frequently fail to produce marketable products. For example, in March 2002, Elan Corporation and Wyeth Ayerst Laboratories announced a decision to cease dosing patients in their Phase 2A clinical trial of their AN-1792 Alzheimer s vaccine containing our QS-21 adjuvant after several patients experienced clinical signs consistent with inflammation in the central nervous system. Several of our agreements also require us to transfer important rights to our collaborators and licensees. As a result of collaborative agreements, we will not completely 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 the programs 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. As a result of these factors, our strategic collaborations may not yield revenue. In addition, 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 equity.

If we are unable to purify heat shock proteins from some cancer types, we may have difficulty successfully completing our clinical trials and, even if we do successfully complete our clinical trials, the size of our potential market could decrease.

Our ability to successfully develop and commercialize Oncophage or AG-858 for a particular cancer type depends 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, including our Phase 3 clinical trials, it may lower the probability of a successful analysis of the data from these trials and, ultimately, the ability to obtain FDA approval. Our overall manufacturing success rate to date for part I of our Phase 3 trial in renal cell carcinoma is 92%; for our Phase 3 trial in metastatic melanoma, it is 70%. Our inability to manufacture adequate amounts of Oncophage

Table of Contents

for approximately 30% of the patients randomized in the Oncophage treatment arm of the metastatic melanoma trial undermines the potential for the trial, as currently designed, to meet its pre-specified clinical endpoints. To address this lower success rate for melanoma, we instituted an inhibitor process to avoid the breakdown of proteins. Subsequent to the implementation of this change, we successfully produced Oncophage for 19 of 25 patients, a success rate of approximately 76%, whereas previously we had produced Oncophage for 123 of 179 patients. The small sample size used subsequent to our process change may make the reported improvement in our manufacturing success unreliable as a predictor of future success.

Based on our completed earlier clinical trials and our ongoing clinical trials conducted in renal cell carcinoma (including our Part I Phase 3 trial), we have been able to manufacture Oncophage from 93% of the tumors delivered to our manufacturing facility; for melanoma (including our Phase 3 trial), 78%; for colorectal cancer, 98%; for gastric cancer, 81%; for lymphoma, 89%; and for pancreatic cancer, 46%. The relatively low rate for pancreatic cancer is due to the abundance of proteases in pancreatic tissue. Proteases are enzymes that break down proteins. These proteases may degrade the heat shock proteins during the purification process. We have made process development advances that have improved the manufacture of Oncophage from pancreatic tissue. In an expanded Phase 1 pancreatic cancer study, Oncophage was manufactured from five of five tumor samples (100%), bringing the aggregate success rate for this cancer type, which was previously 30%, to 46%. We have successfully manufactured AG-858 from approximately 81% of the patient samples received.

We may encounter problems with other types of cancer 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 face claims from patients for whom we are unable to produce a vaccine.

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 at least 80 issued US patents and 112 foreign patents. We also have rights to at least 70 pending US patent applications and 199 pending foreign patent applications. However, our patents may not protect us against our competitors. 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.

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 to, or use, our technology.

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

Table of Contents

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 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.

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 and would consume time and other 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. We know of patents issued to third parties relating to heat shock proteins and alleviation of symptoms of cancer, respectively. We have reviewed these patents, and we believe, as to each claim in those patents, that we either do not infringe the claim or that the claim is invalid. 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 this type of communication, including with respect to the third-party patents mentioned above, as well as a communication alleging infringement of a patent relating to certain gel-fiberglass structures. 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. Additionally, two of the patent applications licensed to us contain claims that are substantially the same as claims in a third-party patent relating to heat shock proteins. We will ask the United States Patent and Trademark Office to declare an interference with this third-party patent, US Patent No. 6,713,608 which we believe is owned by the Science & Technology Corporation @ UNM (University of New Mexico). We believe that the invention of US Patent No. 6,713,608 is the same as that of earlier-filed US Patents No. 5,747,332, 6,066,716, and 6,433,141, which we believe are owned by the University of New Mexico and which were involved in a previous interference proceeding with one of those two applications. During that interference proceeding, we were awarded priority based upon our earlier effective filing date. Accordingly, we believe that the United States Patent and Trademark Office would declare an interference between our pending patent applications and this latest third-party patent and that the claims of US Patent No. 6,713,608 would be deemed invalid. Although we believe that we should prevail against this third-party patent in an interference proceeding, there is no guarantee that that will be the outcome.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to enter into collaborations with other entities or to obtain financing.

If we fail to maintain positive relationships with particular individuals, we may be unable to successfully develop our product candidates, conduct clinical trials, and obtain financing.

Pramod K. Srivastava, Ph.D., a member of our board of directors, the chairman of our scientific and medical advisory board, and a consultant to us, and Garo H. Armen, Ph.D., the chairman of our board of directors and our chief executive officer, who together founded Antigenics in 1994, have been, and continue to be, integral to building the company and developing our technology. If either of these individuals decreases his contributions to the company, our business could be adversely impacted. Dr. Srivastava is not an employee of Antigenics and has other professional commitments. We sponsor research in Dr. Srivastava s laboratory at the University of Connecticut Health Center in exchange for the

Table of Contents

right to license discoveries made in that laboratory with our funding. Dr. Srivastava is a member of the faculty of the University of Connecticut School of Medicine. The regulations and policies of the University of Connecticut Health Center govern the relationship between a faculty member and a commercial enterprise. These regulations and policies prohibit Dr. Srivastava from becoming our employee. Furthermore, the University of Connecticut may modify these regulations and policies in the future to further limit Dr. Srivastava s relationship with us. Dr. Srivastava has a consulting agreement with Antigenics, which includes financial incentives for him to remain associated with us, but these may not prove sufficient to prevent him from severing his relationship with Antigenics, even during the time covered by the consulting agreement. In addition, this agreement does not restrict Dr. Srivastava s ability to compete against us after his association with Antigenics is terminated. This agreement was to expire in March 2005 but was extended for an additional one-year period until March 2006. This agreement will automatically renew for additional one-year periods unless either party decides not to extend the agreement. If Dr. Srivastava were to terminate his affiliation with us or devote less effort to advancing our technologies, we may not have access to future discoveries that could advance our technologies.

We do not have an employment agreement with Dr. Armen. In addition, we do not carry key employee insurance policies for Dr. Armen or any other employee.

We also rely greatly on employing and retaining other highly trained and experienced senior management and scientific personnel. Since our manufacturing process is unique, our manufacturing and quality control personnel are very important. The competition for these and other qualified personnel in the biotechnology field is intense. If we are not able to attract and retain qualified scientific, technical, and managerial personnel, we probably will be unable to achieve our business objectives.

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

Antigenics, our chairman and chief executive officer, Garo H. Armen, Ph.D., and two brokerage firms that served as underwriters in our initial public offering have been named as defendants in a federal civil class action lawsuit. 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 IPO. 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. To date, the plaintiffs have not asserted a specific amount of damages. We have submitted settlement papers with the Federal District Court for the Southern District of New York, which the court preliminarily approved, subject to certain modifications to a proposed bar order regarding potential contribution claims between or among the defendants. There is no guarantee that the settlement will become effective as it is subject to a number of conditions, including the court s final approval. Regardless of the outcome, participation in a lawsuit diverts our management s time and attention from our business and may result in requiring us to pay substantial damages.

In addition, we are involved in other litigation and 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 will be uncertain.

If we fail to obtain adequate levels of reimbursement for our product candidates from third-party payers, the commercial potential of our product candidates will be significantly limited.

Our profitability will depend on the extent to which government authorities, private health insurance providers, and other organizations provide reimbursement for the cost of our product candidates. Many patients will not be capable of paying for our product candidates by themselves. A primary trend in the United States health care industry is toward cost containment. Large private payers, managed care organizations, group purchasing organizations, and similar organizations are exerting increasing influence on decisions regarding the use of particular treatments. Furthermore, many third-party payers limit

Table of Contents

reimbursement for newly approved health care products. Cost containment measures may prevent us from becoming profitable.

It is not clear that public and private insurance programs will determine that Oncophage or our other product candidates come within a category of items and services covered by their insurance plans. For example, although the federal Medicare program covers drugs and biological products, the program takes the position that the FDA s treatment of a product as a drug or biologic does not require the Medicare program to treat the product in the same manner. Accordingly, it is possible that the Medicare program will not cover Oncophage or our other product candidates if they are approved for commercialization. It is also possible that there will be substantial delays in obtaining coverage of Oncophage or our other product candidates and that, if coverage is obtained, there may be significant restrictions on the circumstances in which there would be reimbursement. Where insurance cov