ANTIGENICS INC /DE/
Form 424B5
January 23, 2003

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Filed pursuant to Rule 424(b)(5) and Rule 424(c)
Registration Nos. 333-74002 and 333-90380

PROSPECTUS SUPPLEMENT

(To Prospectus dated August 2, 2002)

6,250,000 Shares

Common Stock

We are selling all of the 6,250,000 shares of common stock offered by this prospectus supplement.

The underwriters are offering 3,450,000 of the shares offered by this prospectus supplement. We are directly offering the remaining 2,800,000 shares to a single existing stockholder.

Our common stock is traded on the Nasdaq National Market under the symbol AGEN. On January 22, 2003, the last reported sale price of our common stock on the Nasdaq National Market was $10.03 per share.

Investing in our common stock involves a high degree of risk. Before buying any shares you should carefully read the discussion of material risks of investing in our common stock in Risk factors beginning on page S-8.

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

	Per share	Total
Public offering price for underwritten shares	$10.00	$34,500,000
Underwriting discounts and commissions on underwritten shares	$ .60	$ 2,070,000
Proceeds, before expenses, to us from underwritten shares	$ 9.40	$32,430,000
Proceeds, before expenses, to us from directly placed shares	$ 9.82	$27,496,000
Proceeds, before expenses, to us from all 6,250,000 shares		$59,926,000

The underwriters may also purchase from us up to an additional 517,500 shares of our common stock at the public offering price less the underwriting discount, to cover over-allotments, if any, within 30 days of the date of this prospectus supplement.

Delivery of the shares will be made on or about January 28, 2003.

UBS Warburg

Needham & Company, Inc.

Morgan Keegan & Company, Inc.

Ryan Beck & Co.

The date of this prospectus supplement is January 23, 2003.

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You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide information different from that contained or incorporated by reference in this prospectus supplement or the accompanying prospectus. Neither the delivery of this prospectus supplement nor the sale of common stock means that information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus is correct after the date of this prospectus supplement. These documents are not an offer to sell or solicitation of an offer to buy these shares of common stock in any circumstance under which the offer or solicitation is unlawful.

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Oncophage®, Aroplatin™, Stimulon™, Quilimmune-P™ and Quilvax-FELV™ are trademarks of Antigenics Inc. Other trademarks included herein are the property of their respective owners.

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Prospectus supplement summary

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the Risk factors section as well as the documents incorporated by reference. Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of the underwriters over-allotment option.

BUSINESS OVERVIEW

We are a biotechnology firm developing products to treat cancers, infectious diseases and autoimmune disorders. Our lead product candidates are: (i) Oncophage®, a personalized therapeutic cancer vaccine in Phase III clinical trials for the treatment of renal cell carcinoma and melanoma, (ii) Aroplatin , a liposomal formulation of a third-generation platinum chemotherapeutic in a Phase II clinical trial for the treatment of colorectal cancer, (iii) AG-858, a personalized therapeutic cancer vaccine in a Phase I clinical trial for the treatment of chronic myelogenous leukemia, and (iv) AG-702/ AG-70X, a therapeutic vaccine program in Phase I development for the treatment of genital herpes.

Oncophage, AG-858 and AG-702/ AG-70X are based on our proprietary heat shock protein technology. Published research suggests that heat shock proteins play a central role in the generation of immune responses against cancer cells and cells infected with viruses and other pathogens. Based on preclinical and clinical studies of our heat shock protein technology, we believe that it will be applicable to all types of cancer and many infectious diseases.

We have generated strong data in multiple human clinical trials using our heat shock protein product candidates, including data demonstrating complete clinical responses in a proportion of patients with measurable metastatic disease in several types of cancer. Additionally, in a proportion of patients who were rendered free of disease by surgery, we have observed prolonged disease-free survival in three different types of cancer. In our studies to date, virtually no toxicity has been observed. We believe that these human data further support the broad applicability and corresponding commercial potential of our heat shock protein product candidates.

LEAD PRODUCT CANDIDATES

Oncophage

Oncophage, our flagship product candidate, is a personalized therapeutic cancer vaccine based on our heat shock protein technology. We initiated a Phase III trial of Oncophage in renal cell carcinoma during the fourth quarter of 2000. This trial is an international, multi-center, randomized, controlled study comparing Oncophage to observation in patients who are at high risk of recurrence after surgical removal of their primary tumor. Study endpoints include recurrence-free survival as well as overall survival. During 2002, we initiated a Phase III trial in metastatic melanoma, and we plan to initiate an additional Phase III study in melanoma during 2003. Oncophage has received fast track designation, as well as orphan drug designation, from the United States Food and Drug Administration (FDA) for both renal cell carcinoma and metastatic melanoma. Other clinical research evaluating Oncophage includes clinical trials for colorectal cancer, gastric cancer, lymphoma and pancreatic cancer.

Heat shock proteins occur naturally in the human body and can function as a transport for the entire antigenic repertoire, or fingerprint , of an individual s cancer. Heat shock proteins also activate powerful cellular immune responses. Oncophage consists of heat shock protein-peptide complexes, or HSPPCs, designed to elicit a T-cell-based immune response to a patient s individual cancer. The HSPPCs in Oncophage are based on a specific heat shock

protein called gp96.

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We manufacture Oncophage from a patient s surgically removed tumor, a portion of which is frozen and shipped to our facility in Massachusetts. After manufacturing Oncophage in a process that takes approximately eight hours per individual patient lot, we formulate Oncophage in sterile saline solution and package it in standard single injection vials. After the performance of stringent quality control testing, including sterility testing, we ship the frozen product back to the hospital where it is administered to the patient in a series of outpatient injections.

Recent Developments

In October 2002, final data from one of our Phase II melanoma trials was published in the *Journal of Clinical Oncology*, the official journal of the American Society of Clinical Oncology (ASCO). This study in patients with metastatic melanoma showed that treatment with Oncophage was associated with objective clinical responses and was generally safe and well tolerated. Out of 28 patients who had residual disease after surgery, two experienced complete clinical responses (complete disappearance of disease) after treatment with Oncophage. The duration of these complete responses was over two years, despite a reported median survival of only seven months for patients with metastatic melanoma. Additionally, three other patients experienced extended disease stabilization (ranging from five to nine months) after treatment with Oncophage. We believe this is one of the first published studies to report complete clinical responses in melanoma patients with extensive metastatic disease after treatment with a non-toxic monotherapy.

During 2002, we made significant progress in the patient enrollment rate of our Phase III renal cell carcinoma trial. At year-end 2001, patient enrollment in this trial was approximately ten percent complete; as of year-end 2002, patient enrollment was approximately 65 percent complete. This increase in enrollment rate has allowed us to increase the statistical power of the study design yet still meet our original target for completed enrollment, which we expect to occur by mid-year 2003.

Aroplatin

Aroplatin is a liposomal formulation of a novel third-generation platinum compound from the family of diaminocyclohexane, or DACH, platinum compounds. During 2002, we initiated a Phase II trial of Aroplatin in advanced colorectal cancer, and we plan to initiate a Phase I/II trial in pancreatic cancer during 2003.

Platinum compounds such as cisplatin and carboplatin are widely-used compounds in cancer chemotherapy. However, current platinum drugs are not always effective because some tumors are resistant to these compounds at the outset of treatment or become resistant during treatment. We expect third-generation platinum chemotherapeutics, like Aroplatin, to overcome some of the resistance seen with earlier generations of platinum chemotherapeutics.

Aroplatin s chemical structure is similar to that of another DACH platinum product Eloxatin (oxaliplatin, Sanofi-Synthelabo), which received FDA approval in August 2002 for the treatment of advanced colorectal cancer. Eloxatin has a significant limitation, however, in that treatment with Eloxatin is associated with significant neurotoxicity a side effect of the nervous system that can cause pain and loss of sensory function in a patient s extremities. In contrast, virtually no neurotoxicity has been reported in clinical testing of Aroplatin. This may be because Aroplatin s active drug ingredient is encapsulated in a liposome. Drugs encapsulated in liposomes have been shown in certain cases to accumulate at the tumor, effecting a higher concentration and longer duration of drug action at the target site (where beneficial effects may occur) while maintaining a lower concentration and shorter duration at other sites (where adverse side effects may occur). In addition, the liposomal delivery system helps to reduce the damaging effects of some drugs on healthy tissues, improving the drug s safety profile. We believe that Aroplatin s liposomal formulation offers a more favorable toxicity profile compared with that of other platinum drugs, including Eloxatin, and may increase the concentration and duration of the active drug ingredient at the tumor site.

With the recent approval of Eloxatin, we initiated a number of head-to-head preclinical experiments in which Aroplatin was compared to Eloxatin. In in vivo studies, Aroplatin had greater anti-tumor

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activity and, in in vitro models of colon and pancreatic cancer, had approximately three times more anti-tumor activity, than Eloxatin.

AG-858

AG-858 is a personalized therapeutic cancer vaccine also based on our heat shock protein technology. AG-858 consists of purified HSPPCs based on a specific heat shock protein called HSP70. In December 2002, we reported interim data from an ongoing pilot Phase I clinical trial combining AG-858 with Gleevec (imatinib mesylate, Novartis) for the treatment of chronic myelogenous leukemia (CML), a type of cancer characterized by the proliferation of abnormal white blood cells. Four of the five evaluable patients in this study were deemed to be unresponsive to treatment with Gleevec alone. After treatment with AG-858, all five evaluable patients showed objective clinical responses, including two patients with complete molecular responses as determined by polymerase chain reaction (PCR), the most sensitive measure available to detect the presence of leukemia cells. In contrast, only ten percent of patients treated with Gleevec alone achieve complete molecular responses as measured by PCR, based on previous reports. In this study, AG-858, like Oncophage, was generally safe and well tolerated. Based on these encouraging data, we intend to initiate one or more Phase II trials of AG-858 in combination with Gleevec during 2003 in CML.

AG-702/ AG-70X

AG-702/ AG-70X is our therapeutic vaccine program for the treatment of genital herpes based on our heat shock protein technology. Genital herpes is a serious, sexually transmitted disease affecting over 85 million people worldwide. Although antiviral drugs are used to alleviate symptoms of the disease, these treatments are not curative and do not prevent the infections from spreading.

AG-702 consists of HSPPCs that we manufacture by complexing a recombinant heat shock protein to a single peptide of herpes simplex virus-2 (HSV-2) and is referred to as a monovalent vaccine. AG-70X is a multivalent vaccine containing in excess of 30 HSV-2 peptides. We believe that by including additional peptides we can design an effective treatment for all HSV-2 patients. AG-70X is an off-the-shelf product candidate that is manufactured synthetically. It is not personalized because the virus that causes genital herpes, HSV-2, is nearly identical in all patients. We are studying AG-702 as a proof of principle in humans and intend to advance the development of the program using AG-70X in future clinical trials.

OUR STRATEGY

Our objective is to become a leading biotechnology firm focused on discovering, developing and commercializing pharmaceutical products for diseases that represent substantial commercial opportunities including cancer, infectious diseases and autoimmune disorders. We plan to achieve this objective by pursuing the following strategies:

Develop and successfully commercialize our cancer products

Our portfolio of cancer products is designed to offer improvements over existing treatments and to improve the quality of life of cancer patients. Oncophage, our most advanced product candidate, is currently being tested in several Phase III and Phase II clinical trials. We intend to market our cancer product candidates using our own specialized sales force in the United States and to engage in collaborations with major pharmaceutical companies in territories outside of the United States.

Advance additional heat shock protein-based products for infectious disease into clinical trials

We are currently focused on the development of a therapeutic vaccine for the treatment of genital herpes using our heat shock protein technology. Building on our experience with AG-702, we intend to advance our multivalent vaccine, AG-70X, into clinical trials. We intend to develop similar vaccines for other infectious diseases. Since large sales organizations will be required for the sale of products in

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these indications, we plan to enter into collaborative agreements with major pharmaceutical companies for the marketing and distribution of these products.

Seek to license or acquire complementary products or technologies

We intend to supplement our internal drug discovery efforts through the acquisition of products and technologies that complement our general product development strategy. Historically, we have made acquisitions of companies that enhanced our product development pipeline. We continue to identify, evaluate and pursue the acquisition or licensing of other strategically valuable organizations or products.

OUR PRODUCT DEVELOPMENT PORTFOLIO

Product		Indication	Status	Commercialization Rights
Our Lead Product Candidates				
	Oncophage® *Personalized therapeutic HSP cancer vaccine*	Renal cell carcinoma	Phase III	Worldwide
		Melanoma	Phase III	
		Colorectal cancer	Phase II	
		Non-Hodgkin s lymphoma	Phase II	
		Gastric cancer	Phase I/II	
		Pancreatic cancer	Phase I	
	Aroplatin *DACH platinum chemotherapeutic*	Colorectal cancer	Phase II	Worldwide
		Pancreatic cancer	Phase I/II[1]	
	AG-858 *Personalized therapeutic HSP cancer vaccine*	Chronic myelogenous leukemia	Phase I	Worldwide
	AG-702/ AG-70X *Therapeutic HSP herpes vaccine*	Genital herpes	Phase I	Worldwide
Our Other Programs[2]				
QS-21 *Vaccine adjuvant*	Various[3]	Phases I-III	Partnered[3]	
Oncophage[NEXGEN] *Next-generation therapeutic HSP cancer vaccine*	Cancers	Preclinical	Worldwide	
CD91 *HSP receptor modulation*	Autoimmune disorders	Preclinical	Worldwide	

HSP-HIV

Therapeutic HSP HIV vaccine
HIV/AIDS Preclinical Worldwide

(1) Enrollment in this trial is expected to commence in 2003.

(2) ATRA-IV, a liposomal all-trans-retinoic acid, is currently being evaluated in a number of cancers.

(3) We have licensed QS-21 to several partners, including GlaxoSmithKline, Wyeth-Lederle, Aventis Pasteur, Elan and Progenics, for use in cancers and infectious diseases. The most advanced program is Progenics vaccine for melanoma, currently in Phase III.

We maintain our operations in Woburn and Framingham, Massachusetts. Our executive offices are in New York, New York. The address for our executive offices is 630 Fifth Avenue, Suite 2100, New York, New York 10111 and our telephone number is (212) 994-8200.

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The offering

Common stock offered:	
Through underwriters	3,450,000 shares
By direct placement	2,800,000 shares
Total	6,250,000 shares
Common stock to be outstanding after the offering	39,363,000 shares
Use of proceeds	We intend to use the net proceeds of this offering to fund additional clinical trials of our lead product candidates and for clinical trials and preclinical studies for our other product candidates; for potential licenses and other acquisitions of complementary technologies and products; and for working capital, capital expenditures and other general corporate purposes. See Use of Proceeds.
Nasdaq National Market Symbol	AGEN

The number of shares of our common stock to be outstanding after this offering in the table above is based on approximately 33,113,000 shares outstanding as of December 31, 2002, and does not include, as of that date:

- 3,997,000 shares of our common stock issuable upon exercise of outstanding options issued under our stock option plans at a weighted average exercise price of $11.84 per share;
- 153,000 shares of common stock issuable upon exercise of outstanding warrants at a weighted average exercise price of $40.69 per share; and
- an additional 1,196,000 shares of common stock available for future issuance under our stock option plans and employee stock purchase plan.

Unless otherwise stated, all information contained in this prospectus supplement assumes that the underwriters do not exercise their over-allotment option.

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Summary consolidated financial data

The table below presents summary consolidated statement of operations and balance sheet data of Antigenics and its subsidiaries. The summary consolidated financial data for the years ended December 31, 1999 through December 31, 2001 are derived from our audited consolidated financial statements for those periods. We derived the summary consolidated financial data as of September 30, 2002 and for the nine months ended September 30, 2001 and 2002 from our unaudited consolidated financial statements. The unaudited consolidated financial statement data includes, in our opinion, all adjustments (consisting only of normal recurring adjustments) that are necessary for a fair presentation of our financial position and results of operations for these periods. Operating results for the nine months ended September 30, 2002 are not necessarily indicative of the results that may be expected for the fiscal year ended December 31, 2002.

This information is only a summary. You should read it in conjunction with our historical consolidated financial statements and related notes incorporated by reference in this prospectus supplement and on file with the SEC. For more details on how you can obtain our SEC reports incorporated by reference herein, you should read the section of the prospectus entitled Where You Can Find More Information.

Consolidated statement of operatis data:	Year ended December 31,			Nine months ended September 30,	
	1999	2000	2001	2001	2002
	(in thousands, except per share data)			(unaudited)	
Revenue	$581	$443	$4,555	$2,956	$2,607
Expenses:					
Cost of sales	(363)	(1,064)	(688)	(992)	
Research and development	(11,958)	(17,575)	(31,357)	(21,605)	(28,485)
General and administrative	(7,480)	(9,190)	(13,762)	(10,338)	(13,687)
Acquired in-process research and development [1]		(25,800)	(34,596)	(32,436)	
Operating loss	(18,857)	(52,485)	(76,224)	(62,111)	(40,557)
Interest income, net	723	5,756	2,683	2,416	935
Other income (expense), net	10		(41)	73	

Net loss[2][3]	$(18,124)	$(46,729)	$(73,541)	$(59,736)	$(39,549)
Net loss per share, basic and diluted	$(1.00)	$(1.90)	$(2.61)	$(2.14)	$(1.20)
Weighted average number of shares outstanding, basic and diluted	18,144	24,659	28,143	27,852	32,844

	As of September 30, 2002	
Consolidated bnce sheet data: (in thousands)	**Actual**	**As Adjusted[4]**

		(unaudited)
Cash, cash equivalents and short-term investments	$70,464	$130,020
Total current assets	75,812	135,368
Total assets	103,998	163,554
Total current liabilities	9,683	9,683
Long-term liabilities, less current portion	1,104	1,104
Stockholders equity	93,211	152,767

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(1) We recorded non-recurring charges to operations for the write-off of in-process research and development acquired in our mergers with Aquila Biopharmaceuticals, Inc. in November 2000 and Aronex Pharmaceuticals, Inc. in July 2001.

(2) Prior to our conversion from a limited liability company to a corporation in February 2000, in accordance with federal, state and local income tax regulations which provide that no income taxes are levied on United States limited liability companies, each member of the limited liability company was individually responsible for reporting his share of the company s net income or loss. Accordingly, we have not provided for income taxes in our consolidated financial statements for periods before February 2000. Given our history of incurring operating losses, no income tax benefit is recognized in our consolidated financial statements for periods after February 2000 because of a loss before income taxes and the need to recognize a valuation allowance on net deferred tax assets.

(3) Effective July 1, 2002, Antigenics adopted Statement of Financial Accounting Standards (SFAS) No. 141, Business Combinations and effective January 1, 2002 adopted SFAS No. 142, Goodwill and Other Intangibles. As a result, we have not amortized the goodwill associated with our July 2001 acquisition of Aronex Pharmaceuticals and have ceased amortization of all goodwill beginning January 1, 2002. Had SFAS No. 142 been adopted by us effective January 1, 2000, net loss and net loss per share, basic and diluted, would have been as follows (in thousands, except per share data):

	Year ended December 31,		Nine months ended September 30,
	2000	**2001**	**2001**
Net loss, as reported	*$(46,729)*	*$(73,541)*	*$(59,736)*
Goodwill amortization and assembled workforce amortization	*39*	*480*	*360*
Pro forma net loss	*$(46,690)*	*$(73,061)*	*$(59,376)*
Net loss per share, basic and diluted, as reported	*$(1.90)*	*$(2.61)*	*$(2.14)*
Pro forma net loss per share, basic and diluted	*$(1.89)*	*$(2.60)*	*$(2.13)*

(4) As adjusted to give effect to our sale of the 6,250,000 shares of common stock offered hereby, after deducting the underwriting discounts and commissions (with respect to those shares being sold through the underwriters) and estimated offering expenses payable by us, as though this sale occurred as of September 30, 2002.

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Risk factors

You should carefully consider the following risk factors before you decide to purchase our common stock. Any of these risks could have a material adverse impact on our business, financial condition, operating results or cash flows. This could cause the trading price of our common stock to decline, and you may 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 September 30, 2002, we have generated net losses totaling $197 million, including $40 million during the first nine months of 2002. We expect to incur increasing and 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 III clinical trials are particularly expensive to conduct. We do not expect to generate significant revenues for several years. To date, we have generated product sales revenue from only one product, our feline leukemia vaccine named Quilvax-FELV. Our revenues from Quilvax-FELV were $1.9 million for the nine-months ended September 30, 2002. These revenues are generated through sales of Quilvax-FELV to our marketing partner Virbac, S.A. This agreement expired in 2002, and we are negotiating its renewal with Virbac. Any regulatory, marketing or other difficulties we experience with Quilvax-FELV, including non-renewal of our agreement with Virbac, could jeopardize that revenue stream.

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 September 30, 2002, we had approximately $70 million in cash, cash equivalents and short-term investments. With our current working capital and the estimated net proceeds from this offering, we expect that we could fund our development programs, clinical trials, and other operating expenses into the third quarter of 2004. We plan to raise additional funds prior to that time. Since our inception, we have financed our operations primarily through the sale of equity, interest income earned on cash, cash equivalent balances and short-term investments and debt provided through a credit facility secured by some of our manufacturing and laboratory assets. In order to fund our future needs, 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 may 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 lead cancer vaccine, Oncophage. We also may be forced to license technologies to others that allocate to third parties substantial portions of the potential value of these technologies.

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 products by continuing our existing collaborative arrangements with academic and corporate collaborators and licensees and by entering into new collaborations. Our success depends on our ability to successfully negotiate such agreements and on the success of the other parties in performing research, preclinical and clinical testing. Our collaborations involving QS-21, for example, depend on our partners 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 permanently cease dosing patients in their Phase IIA clinical trial of their lead Alzheimer s

vaccine containing QS-21. Several of our agreements also require us to transfer important rights to our collaborators and licensees. These 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 program or elect to collaborate with a different company. 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 revenues. 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 securities.

We must receive separate regulatory approvals for each of our drugs and vaccines in each type of disease before we can market and sell them in the United States or internationally and this approval process is uncertain, time-consuming and expensive.

We and our collaborators cannot sell any drug or vaccine until it receives regulatory approval from federal, state and local governmental authorities in the United States, including the FDA, and from similar agencies in other countries. Oncophage and any other drug candidate could take a significantly longer time to gain regulatory approval than we expect or may never gain approval. 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 flagship product candidate, Oncophage, is a novel cancer therapeutic vaccine that is personalized for each patient. To date, the FDA and foreign regulatory agencies have approved only a limited number of cancer therapeutic vaccines for commercial sale and have relatively little experience in reviewing personalized medicine therapies. This lack of experience may lengthen the regulatory review process for Oncophage, increase our development costs and delay or prevent commercialization.

To obtain regulatory approvals, we must, among other requirements, complete carefully controlled and well-designed clinical trials demonstrating that a particular drug or vaccine 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 of clinical trials or the ability to interpret the data from the trials; we could encounter similar problems. The timing and success of a clinical trial is dependent on enrolling sufficient patients in a timely manner, avoiding adverse patient reactions, and demonstrating in a scientifically significant manner the efficacy of a product. We rely on third party clinical investigators to conduct our clinical trials and as a result, we may encounter delays outside our control. Future clinical trials may not show that our drugs and vaccines are safe and effective. In addition, we or the FDA might delay or halt the clinical trials, including our Phase III trials of Oncophage, for various reasons, including:

- failure to comply with extensive FDA regulations;
- the product may not appear to be more effective than current therapies;
- the product may have unforeseen or significant adverse side effects or other safety issues;
- the time required to determine whether the product is effective may be longer than expected;
- we may be unable to adequately follow or evaluate patients after treatment with the product;

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;

sufficient numbers of patients may not enroll in our clinical trials; or

we may be unable to produce sufficient quantities of the product 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 approval or clearances for our drugs or vaccines 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 products in a timely manner, we will not be able to commercialize them, and therefore, our business and stock price will suffer.

Even if we receive regulatory approval for our products, the FDA may impose limitations on the indicated uses for which our products may be marketed. These limitations could reduce 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 our marketing applications and criminal prosecution.

If we are unable to purify heat shock proteins from some cancer types, the size of our potential market would decrease.

Heat shock proteins occur naturally in the human body and activate powerful cellular immune responses. Our ability to successfully commercialize Oncophage for a particular cancer type depends on our ability to purify heat shock proteins from that type of cancer. Based on our clinical trials conducted to date, in renal cell carcinoma, we have been able to manufacture Oncophage from 93% of the tumors delivered to our manufacturing facility; for melanoma, 89%; for colorectal cancer, 98%; for gastric cancer, 81%; for lymphoma, 86%; and for pancreatic cancer, 30%. 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 recently made process development advances that have improved the manufacture of Oncophage from pancreatic tissue. In an expanded Phase I pancreatic cancer study, Oncophage was manufactured from five of five tumor samples (100%), bringing the aggregate success rate for this cancer type to 46%.

We may encounter this problem or similar problems with other types of cancers as we expand our research. If we cannot overcome these problems, the number of cancer types that Oncophage could treat would be limited.

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 more than 72 issued United States patents and 114 foreign patents. We also have rights to more than 49 pending United States patent applications and 99 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 in court, is uncertain. In addition, the type and extent of patent claims that will be issued to us in the future is uncertain. Any patents which are issued may not contain claims which will 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 the 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 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 ground that such other party s activities are not covered by (that is, do not infringe) our patents.

Furthermore, a third party may claim that we are using inventions covered by such third party s patents 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 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 the patents, that we either do not infringe the claim of the patents 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 biotech companies, have received this type of communication, including with respect to the third party patents mentioned above. 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, and we may not be able to do this. 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, one of the patent applications licensed to us contains claims that are substantially the same as claims in three of the third party patents mentioned above. The United States Patent and Trademark Office has declared an interference proceeding with respect to two of these third party patents to resolve this conflict. In an interference proceeding, the party with the earliest effective filing date has certain advantages. Although we believe that our claims have an earlier effective filing date than the conflicting claims of the other patents, if this third party were to prevail in the

interference proceeding, it could result in abandonment of our patent application and the potential need to seek a license from this party which may not be available on reasonable terms, if at all.

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 continue our operations.

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 civil class action lawsuit filed on November 5, 2001 in the Federal District Court in the Southern District of New York. Dr. Armen was dismissed without prejudice from these claims in October 2002. The suit alleges that these underwriters 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 underwriters customers based upon an agreement by such customers to purchase additional shares of our stock in the secondary market. We could be required to pay substantial damages and, regardless of the outcome, the lawsuit may cause a diversion of our management s time and attention from our business.

In addition, we may become involved in additional litigation with our commercial partners or with others. Any such litigation could be expensive in terms of out-of-pocket c