ANTIGENICS INC /DE/
Form S-3/A
December 16, 2004

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As filed with the Securities and Exchange Commission on December 15, 2004

Registration No. 333-118171

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Amendment No. 3
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 registrant s 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 M. 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, as amended (the Securities Act) 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 number of 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 or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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The information in the prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and we are not soliciting an offer to buy these securities in any state where an offer is not permitted.

Subject to Completion and Amendment, dated December 15, 2004

PROSPECTUS

350,000 Shares

Antigenics Inc.

Antigenics Common Stock

This prospectus relates to the resale of 350,000 shares of Antigenics common stock, $0.01 par value per share, that we issued in a private placement on July 30, 2004 in connection with our acquisition of assets from Mojave Therapeutics, Inc. These shares may be offered and sold from time to time by the selling securityholders listed in this prospectus. We will not receive any of the proceeds from the sale of these shares.

Our common stock trades on the Nasdaq National Market under the symbol AGEN.

Investing in Antigenics securities involves a high degree of risk. Before purchasing shares of Antigenics common stock, you should carefully read and consider the risk factors identified under Risk Factors beginning on page 3.

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

The mailing address at our principal offices is 630 Fifth Avenue, Suite 2100, New York, New York 10111. Our telephone number at these offices is 212-994-8200.

The date of this prospectus is , 2004.

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Oncophage® and Aroplatin™ are trademarks of Antigenics Inc. Other trademarks included in this prospectus are the property of their owners.

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RISK FACTORS

If you purchase Antigenics securities, you will take on financial risk. In deciding whether to invest, you should carefully analyze the following risk factors in addition to the other information included and incorporated by reference in this prospectus. It is especially important to consider these risk factors when you read forward-looking statements.

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

From our inception through September 30, 2004, we have generated net losses totaling $318 million. Our net losses for the nine months ended September 30, 2004, and for the years ended December 31, 2003, 2002, and 2001 were $38.7 million, $65.9 million, $55.9 million, and $73.5 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 we plan to initiate two new Phase 3 clinical trials; during 2004, in renal cell carcinoma and during 2005 in melanoma. Furthermore, our ability to generate cash from operations is dependent on if and when we will be able to commercialize our products. We expect that the earliest we may be able to commercialize Oncophage would be in late 2005. 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 September 30, 2004, we had approximately $106.3 million in cash, cash equivalents and short-term investments. In February 2004, we sold 5,400,000 shares of our common stock, raising net proceeds of approximately $54 million. With our current capital we expect that we could fund our development programs, clinical trials, and other operating expenses through at least the end of 2005. We plan to raise additional funds prior to that time. For the nine months ended September 30, 2004, the sum of our average monthly cash used in operating activities plus our average monthly capital expenditures was approximately $5.2 million. Total capital expenditures for the nine months ended September 30, 2004 were $2.4 million. We anticipate additional capital expenditures of up to $2.6 million during the remainder of 2004. 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.

Because the FDA has indicated 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. Product characterization represents our products specifications for purity, identity, potency and pH. On October 24, 2003, we submitted to the FDA specifications for purity, identity, potency and pH, which represent product characterization data, and on November 24, 2003, we announced that the FDA had 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 (trial C-100-12) and our Phase 3 trial in melanoma (trial C-100-21), 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

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Oncophage provided to patients before December 2003 as 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 have addressed the comments the FDA raised in connection with the partial clinical hold. After the clinical hold was lifted, we were asked by the FDA 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 our validation package to the FDA for the qualified potency assays, and we are awaiting their response. 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 FDA may request changes in the validation package, and we will incorporate all agreed upon changes in the final validation package.

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 intend to expand our clinical development plan by initiating a second part to this Phase 3 trial in a similar patient population. The FDA has approved this registration plan, which comprises two components part I and part II. The FDA has indicated 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, while part II of the study is continuing. We expect to support this position with data which may demonstrate that Oncophage used in part I of the study be considered sufficiently characterized. We would expect to derive that data from additional tests we plan to perform on frozen portions of the administered product. We plan to complete such tests if and when the FDA accepts the validation of our qualified assays for potency. 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 given (1) part I of our Phase 3 renal cell carcinoma trial is designed to show that patients being treated with Oncophage have approximately a 44% recurrence-free survival advantage over patients in the observation arm, which we believe would be regarded as a substantial benefit in this patient population, (2) Oncophage has 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 the companies complete confirmatory studies. We are not aware of other biological products approved by the FDA where these products were considered by the FDA to be insufficiently characterized. However, as noted previously, we plan to perform additional tests of Oncophage product samples produced prior to December 2003 and attempt to demonstrate that our product should be considered sufficiently characterized. There is no assurance that we will be successful in demonstrating that our product is sufficiently characterized or that the FDA would accept such a strategy.

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 is likely continue to adhere to its current position that the data from this part of the trial cannot, by itself, support a BLA. 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 3 years and cost between

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$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 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 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 (C-100-21). 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. We did not discuss our regulatory strategy for melanoma during our type A meeting with the FDA to discuss renal cell carcinoma. 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 our ongoing Phase 3 clinical trial of Oncophage in the treatment of 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. Our Phase 3 renal cell carcinoma trial is designed to show that patients in the Oncophage arm have approximately a 44% recurrence-free survival advantage over the patients in the observation arm. We believe that this would be regarded as a substantial benefit in this patient population. We interpreted the recommendation by the DMC that we would not need to add patients in order to potentially achieve a 44% recurrence-free survival advantage 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 is preliminary. The final data from the trial may not demonstrate efficacy and safety. 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 cancer therapeutic vaccine that is personalized for each patient. To date, the FDA has not approved any cancer therapeutic vaccines for

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commercial sale, and foreign regulatory agencies have approved only a limited number. Both the FDA and foreign regulatory agencies, particularly 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 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 have not held discussions with regulatory agencies other than the FDA regarding product approval strategies. As of September 30, 2004, we have spent approximately 10 years and $161 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 plan to initiate part II of our Phase 3 trial for Oncophage in renal cell carcinoma in early 2005. During 2005, we also intend to initiate a second Phase 3 trial in melanoma. Even after reviewing the 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 or melanoma. 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 adverse patient reactions and demonstrating in a statistically significant manner the safety and efficacy of the product candidate. 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 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, and/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 second Phase 3 trial in melanoma that we plan to initiate during 2005. In addition, the FDA may request additional information or data to which we do not have access. 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.

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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 products 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 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 or may gain approval for only limited indications.

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 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 trails, 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 drop-out rate in a trial may undermine the ability to gain statistically significant data from the study.

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If new data from our research and development activities continue 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.

We will not generate further product sales revenue from Quilvax-FELV.

To date, we have generated product sales revenue from only one product, a feline leukemia vaccine, the manufacturing rights to which we sold in March 2004 to Virbac, S.A., our former marketing partner. Prior to the sale, our revenues from the feline leukemia vaccine for the nine months ended September 30, 2004 and the years ended December 31, 2003, 2002, and 2001 were $0.3 million, $3.5 million, $2.6 million, $1.6 million, respectively. We no longer sell that product.

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, 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 products to market. These collaborators and licensees could choose not to devote resources to these arrangements or,

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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 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 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 would decrease.

Heat shock proteins occur naturally in the human body and have the potential to activate powerful cellular immune responses. 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 our Phase 3 trial, C-100-12, in renal cell carcinoma is 92%; for our Phase 3 trial in metastatic melanoma, C-100-21, it is 70%. Our inability to manufacture adequate amounts of Oncophage for approximately 30% of the patients randomized to date in the Oncophage treatment arm of the melanoma trial will jeopardize 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 18 of 23 patients, a success rate of approximately 78%, 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 C-100-12 trial), we have been able to manufacture Oncophage from 93% of the tumors delivered to our manufacturing facility; for melanoma (including our C-100-21 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 cancers 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 U.S. patents and 85 foreign patents. We also have rights to at least 67 pending U.S. patent applications and 189 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

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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 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 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 biotechnology 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, 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, U.S. Patent No. 6,713,608 which we believe is owned by the Science & Technology Corporation @ UNM. We believe that the invention of U.S. Patent No. 6,713,608 is the same as that of earlier-filed U.S. 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 should declare an interference between our pending patent applications and this latest third-party patent and that the claims of U.S. Patent No. 6,713,608 should 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

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the initiation and continuation of any litigation could have a material adverse effect on our ability to enter into collaborations with other entities.

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 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 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 expires in March 2005 but will be automatically extended 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 stock offering. The suit also alleges that shares of our stock were allocated to certain of the investment banking firms customers based upon agreements by such customers to purchase additional shares of our stock in the secondary market. 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; however, a failure to finalize a settlement could require us to pay substantial damages. Regardless of the outcome, participation in a lawsuit may cause a diversion of our management s time and attention from our business.

In addition, we are involved in other litigation, and may become involved in additional litigation, with former employees, our commercial partners, and others. 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.

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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 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 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 coverage is available, there may be limits on the payment amount. Congress and the Medicare program periodically propose significant reductions in the Medicare reimbursement amounts for drugs and biologics. Such reductions could have a material adverse effect on sales of any of our product candidates that receive marketing approval. In December 2003, the President of the United States signed the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. The future impact of this legislation on our product candidates is uncertain. Effective January 1, 2004, Medicare payments for many drugs administered in physician s offices were reduced significantly. This provision impacts many drugs used in cancer treatment by oncologists and urologists. The payment methodology changes in future years, and it is unclear how the payment methodology will impact reimbursement for Oncophage, if it receives regulatory approval, and incentives for physicians to recommend Oncophage relative to alternative therapies.

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

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

decreased demand for our product candidates;

injury to our reputation;

withdrawal of clinical trial volunteers;

costs of related litigation; and

substantial monetary awards to plaintiffs.

We manufacture Oncophage and AG-858 from a patient s cancer cells, and a medical professional must inject Oncophage or AG-858 into that same patient. A patient may sue us if we, a hospital, or a delivery company fails to deliver the removed cancer tissue or that patient s Oncophage or AG-858. We anticipate that the logistics of shipping will become more complex if the number of patients we treat increases, and it is possible that all shipments will not be made without incident. In addition, administration of Oncophage or AG-858 at a hospital poses risk of delivery to the wrong patient. Currently, we do not have insurance that covers loss of or damage to Oncophage or AG-858, and we do not know whether insurance will be available to us at a reasonable price or at all. We have limited product liability coverage for clinical research use of product

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candidates. Our product liability policy provides $10 million aggregate coverage and $10 million per occurrence. This limited insurance coverage may be insufficient to fully compensate us for future claims.

We may incur significant costs complying with environmental laws and regulations.

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

Although we believe that our current procedures and programs for handling, storage, and disposal of these materials comply with federal, state, and local laws and regulations, we cannot eliminate the risk of accidents involving contamination from these materials. Although we have limited pollution liability coverage ($2 million) and a workers compensation liability policy, in the event of an accident or accidental release, we could be held liable for resulting damages, which could be substantially in excess of any available insurance coverage and could substantially disrupt our business.

Our competitors in the biotechnology and pharmaceutical industries may have superior products, manufacturing capability or marketing expertise.

Our business may fail because we face intense competition from major pharmaceutical companies and specialized biotechnology companies engaged in the development of product candidates and other therapeutic products, including heat shock proteins directed at cancer, infectious diseases, autoimmune disorders, and degenerative disorders. Several of these companies have products that utilize similar technologies and/or personalized medicine techniques, such as CancerVax s Canvaxin, currently in a Phase 3 trial for melanoma and a Phase 2 trial in colon cancer, Dendreon s Provenge, with fast track designation and currently in a Phase 3 trial for prostate cancer, and Mylovenge in a Phase 2 trial for multiple myeloma, Stressgen s HspE7 currently in a Phase 2 trial in HPV- internal genital warts, AVAX s M-Vax in melanoma, L-Vax currently in Phase 2 trials for acute myelogenous leukemia (AML) and O-Vax, currently in a Phase 2 for ovarian cancer, Intracel s OncoVax, currently approved for administration in the Netherlands, Switzerland and Israel and in a Phase 3 trial in the US for colon cancer, and Cell Genesys GVAX vaccines currently in trials for prostate (Phase 3), AML (Phase 2), pancreas (Phase 2), lung cancer (Phase 2), and myeloma (Phase 1/2). Patents have been issued in both the U.S. and Europe related to Stressgen s heat shock protein technology. In particular, U.S. patents 6,524,825, 6,338,952 and 6,335,183; and European patents EP700445 and EP1002110 are issued. Additionally, many of our competitors, including large pharmaceutical companies, have greater financial and human resources and more experience than we do. Our competitors may:

commercialize their products sooner than we commercialize our own;

develop safer or more effective therapeutic drugs or preventive vaccines and other therapeutic products;

implement more effective approaches to sales and marketing;

establish superior intellectual property positions; or

discover technologies that may result in medical insights or breakthroughs which render our drugs or vaccines obsolete, possibly before they generate any revenue.

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More specifically, if we receive regulatory approvals, some of our product candidates will compete with well-established, FDA-approved therapies such as interleukin-2 and interferon-alpha for renal cell carcinoma and melanoma, which have generated substantial sales over a number of years. We anticipate that we will face increased competition in the future as new companies enter markets we seek to address and scientific developments surrounding immunotherapy and other cancer therapies continue to accelerate.

Risks Related to our Common Stock

Our officers and directors may be able to block proposals for a change in control.

Antigenics Holdings L.L.C. is a holding company that owns shares of our common stock and as of September 30, 2004, Antigenics Holdings L.L.C. controlled approximately 25% of our outstanding common stock. Due to this concentration of ownership, Antigenics Holdings L.L.C. may be able to prevail on all matters requiring a stockholder vote, including:

the election of directors;

the amendment of our organizational documents; or

the approval of a merger, sale of assets, or other major corporate transaction.

Certain of our directors and officers directly and indirectly own approximately 74% of Antigenics Holdings L.L.C. and, if they elect to act together, can control Antigenics Holdings L.L.C. In addition, several of our directors and officers directly and indirectly own approximately 4% of our outstanding common stock.

A single, otherwise unaffiliated, stockholder holds a substantial percentage of our outstanding capital stock.

According to publicly filed documents, Mr. Brad M. Kelley beneficially owns 5,546,240 shares of our outstanding common stock and 31,620 shares of our Series A convertible preferred stock. The shares of preferred stock are currently convertible at any time into 2,000,000 shares of common stock at an initial conversion price of $15.81, are non-voting, and carry a 2.5% annual dividend yield. If Mr. Kelley had converted all of the shares of preferred stock on September 30, 2004, he would have held approximately 16% of our outstanding common stock. We currently have a right of first refusal agreement with Mr. Kelley that provides us with limited rights to purchase certain of Mr. Kelley s shares if he proposes to sell them to a third party.

Mr. Kelley s substantial ownership position provides him with the ability to substantially influence the outcome of matters submitted to our stockholders for approval. Furthermore, collectively, Mr. Kelley and Antigenics Holdings L.L.C. control approximately 37% of our outstanding common stock, providing substantial ability, if they vote in the same manner, to determine the outcome of matters submitted to a stockholder vote. If Mr. Kelley were to convert all of his preferred stock into common stock, the combined percentage would increase to 39%. Additional purchases of our common stock by Mr. Kelley also would increase both his own percentage of outstanding voting rights and the percentage combined with Antigenics Holdings L.L.C. (Mr. Kelley s shares of preferred stock do not carry voting rights; the common stock issuable upon conversion, however, carries the same voting rights as other shares of common stock.)

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

Our certificate of incorporation and bylaws contain provisions that could make it more difficult for a third party to acquire us without consent of our board of directors. Our certificate of incorporation provides for a staggered board and removal of directors only for cause. Accordingly, stockholders may elect only a minority of our board at any annual meeting, which may have the effect of delaying or preventing changes in management. In addition, under our certificate of incorporation, our board of directors may issue shares of preferred stock and determine the terms of those shares of stock without any further action by our stockholders. Our issuance of preferred stock could make it more difficult for a third party to acquire a

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majority of our outstanding voting stock and thereby effect a change in the composition of our board of directors. Our certificate of incorporation also provides that our stockholders may not take action by written consent. Our bylaws require advance notice of stockholder proposals and nominations, and permit only our president or a majority of the board of directors to call a special stockholder meeting. These provisions may have the effect of preventing or hindering attempts by our stockholders to replace our current management. In addition, Delaware law prohibits a corporation from engaging in a business combination with any holder of 15% or more of its capital stock until the holder has held the stock for three years unless, among other possibilities, the board of directors approves the transaction. The board may use this provision to prevent changes in our management. Also, under applicable Delaware law, our board of directors may adopt additional anti-takeover measures in the future.

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

Between our initial public offering on February 4, 2000 and October 22, 2004, and for the twelve and six months ended October 22, 2004, the closing price of our common stock has fluctuated between $4.72 and $52.63 per share, $4.72 and $12.48, and $4.72 and $10.36 per share, respectively, with an average daily trading volume for the nine months ended September 30, 2004 of approximately 446,000 shares. The market has experienced significant price and volume fluctuations that are often unrelated to the operating performance of individual companies. In addition to general market volatility, many factors may have a significant adverse effect on the market price of our stock, including:

announcements of decisions made by public officials;

results of our preclinical and clinical trials;

announcements of technological innovations or new commercial products by us or our competitors;

developments concerning proprietary rights, including patent and litigation matters;

publicity regarding actual or potential results with respect to products under development by us or by our competitors;

regulatory developments; and

quarterly fluctuations in our financial results.

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

The sale by us or the resale by stockholders of a significant number of shares of our common stock could cause the market price of our common stock to decline. As of September 30, 2004, we had approximately 45,487,000 shares of common stock outstanding. All of these shares are eligible for sale on the NASDAQ National Market, although certain of the shares are subject to sales volume and other limitations.

We have filed registration statements to permit the sale of 10,436,831 shares of common stock under our equity incentive plan, and certain equity plans that we assumed in the acquisitions of Aquila Biopharmaceuticals, Inc. and Aronex Pharmaceuticals, Inc. We have also filed a registration statement to permit the sale of 300,000 shares of common stock under our employee stock purchase plan. We have also filed a registration statement to permit the sale of 100,000 shares of common stock under our directors deferred compensation plan. As of September 30, 2004, options to purchase approximately 5,019,000 shares of our common stock upon exercise of options with a weighted average exercise price per share of $9.80 were outstanding. Many of these options are subject to vesting that generally occurs over a period of up to five years following the date of grant. As of September 30, 2004, warrants to purchase approximately 92,000 shares of our common stock with a weighted average exercise price per share of $40.69 were outstanding. On November 2, 2004, we filed a registration statement relating to the resale of 350,000 shares of our common stock that we issued in a private placement on July 30, 2004 in connection with our acquisition of assets from Mojave Therapeutics, Inc. Once that registration statement becomes effective, those shares may be offered and sold from time to time by the selling securityholders listed in the related prospectus. The market price of our common stock may decrease based on the expectation of such sales. Similarly, on November 2, 2004, we filed a registration statement with

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respect to an aggregate of $100 million of our common stock, preferred stock, and debt. The market price of our common stock may decrease based on investor expectations that we will issue a substantial number of shares of common stock or securities convertible into common stock at low prices.

Because we are a relatively small company and are cash flow negative, we expect to be disproportionately negatively impacted by recently enacted changes in the securities laws and regulations, which are likely to increase our costs and require additional management resources.

The Sarbanes-Oxley Act of 2002, which became law in July 2002, has required changes in some of our corporate governance, securities disclosure and compliance practices. In response to the requirements of that Act, the SEC and the Nasdaq have promulgated new rules and listing standards covering a variety of subjects. Compliance with these new rules and listing standards has significantly increased our legal and financial and accounting costs, and we expect these increased costs to continue. In addition, the requirements have taxed a significant amount of management s and the Board of Directors time and resources. Likewise, these developments may make it more difficult for us to attract and retain qualified members of our board of directors, particularly independent directors, or qualified executive officers. Because we are a relatively small company and are cash flow negative, we expect to be disproportionately negatively impacted by these changes in securities laws and regulations which will increase our costs, require additional management resources and may, in the event that we receive anything other than an unqualified report on our internal controls over financial reporting, result in greater difficulty in raising funding for our operations and negatively impact our stock price.

As directed by Section 404 of the Sarbanes-Oxley Act of 2002, the SEC adopted rules requiring public companies to include a report of management on the company s internal controls over financial reporting in their annual reports on Form 10-K that contains an assessment by management of the effectiveness of the company s internal controls over financial reporting. In addition, the public accounting firm auditing the company s financial statements must attest to and report on management s assessment of the effectiveness of the company s internal controls over financial reporting. This requirement will first apply to our annual report on Form 10-K for our fiscal year ending December 31, 2004. If we are unable to conclude that we have effective internal controls over financial reporting or, if our independent auditors are unable to provide us with an unqualified report as to the effectiveness of our internal controls over financial reporting as of December 31, 2004 and future year-ends as required by Section 404 of the Sarbanes-Oxley Act of 2002, investors could lose confidence in the reliability of our financial statements, which could result in a decrease in the value of our securities. We are a small company with limited resources. The number and qualifications of our finance and accounting staff are limited, and we have limited monetary resources. We experience difficulties in attracting qualified staff with requisite expertise due to the profile of our company and a generally tight market for staff with expertise in these areas. Furthermore, guidance from relevant regulatory bodies and others in the field is evolving and being refined on an ongoing basis, creating difficulties in attempting to assure all matters are addressed in a timely manner as the year end deadline approaches. As of mid-December 2004, we are attempting to finalize our testing and evaluation of our internal controls over financial reporting, with a goal of remediating any identified deficiencies. A key risk is that we will not have adequate time to remediate identified deficiencies prior to year end.

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NOTE REGARDING FORWARD-LOOKING STATEMENTS

This information statement contains forward-looking statements. Generally, these statements can be identified by the use of terms like believe, expect, anticipate, plan, may, will, could, estimate, potential, opportunity, future, project and similar terms. For may include statements about our time lines for completing clinical trials, time lines for releasing data from clinical trials, time lines for initiating new clinical trials, expectations regarding clinical trials and regulatory processes, expectations regarding test results, future product research and development activities, the expected effectiveness of therapeutic drugs and vaccines in treating diseases, applicability of our heat shock protein technology to multiple cancers and infectious diseases, competitive position, plans for regulatory filings, possible receipt of future regulatory approvals, expected cash needs, plans for sales and marketing, implementation of corporate strategy and future financial performance. These forward-looking statements involve a number of risks and uncertainties that could cause actual results to differ materially from those suggested by the forward-looking statements. These risks and uncertainties include, among others, that clinical trials may not demonstrate that our products are both safe and more effective than current standards of care; that we may be unable to obtain the regulatory approvals necessary to conduct additional clinical trials; that we may not be able to enroll sufficient numbers of patients in our clinical trials; that we may be unable to obtain the regulatory approvals necessary to commercialize our products because the FDA or other regulatory agencies are not satisfied with our trial protocols or the results of our trials; that we may fail to adequately protect our intellectual property or that we are determined to infringe on the intellectual property of others; changes in financial markets and geopolitical developments; and the solvency of counter-parties under subleases and general real estate risks. Forward-looking statements, therefore, should be considered in light of all of the information included or referred to in this information statement, including the information set forth under the heading RISK FACTORS beginning on page 3.

You are cautioned not to place significant reliance on these forward-looking statements, which speak only as of the date of this information statement. We undertake no obligation to update these statements.

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BUSINESS

Overview

We are a biotechnology firm developing products to treat cancers, infectious diseases and autoimmune disorders. Our most advanced product candidate is Oncophage®, a personalized 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 for metastatic melanoma. Our product candidate portfolio also includes (1) AG-858, a personalized 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. Our related business activities include research and development, regulatory and clinical affairs, business development, 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 of tumor lesions (a partial response) 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 a favorable safety profile. The most common side effects have been mild-moderate injection site reactions and transient low-grade fevers. We believe that these human data further support 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, or 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 (HSP70) attached to a single peptide, or protein fragment, of 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 peptides. We initiated 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 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 IND filing. Delays in animal experiments are common. 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.

Our other product candidates and clinical programs include Aroplatin, a novel liposomal third-generation platinum chemotherapeutic that has been studied in two Phase 1 trials of patients with colorectal cancer and 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 a lipid or fatty substance. Our

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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 from much smaller tumor tissue samples. We are also studying pathways through which heat shock proteins activate the immune system as well as combinations of Oncophage and other compounds.

Heat Shock Protein Technology

Heat shock proteins, or 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. Antigens or antigenic peptides are portions of proteins which stimulate an immune response. Because HSPs chaperone peptides, HSPs bind to the broad array of antigens, or antigenic fingerprint of the cell in which they reside.

Although heat shock proteins are normally found inside cells, they also serve an important purpose when found extracellularly, or 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 key to our technology. The chaperoning nature of heat shock proteins allows us to produce vaccines containing all 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 the broad array of peptides produced by that patient s tumor. These heat shock protein-peptide complexes, or 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.

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 (HSP70) 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.

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Product Development Portfolio

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

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

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

(2) These trials are closed to enrollment.

(3) We do not intend to initiate new clinical trials of Aroplatin until we complete our review of this program.

Oncophage

Introduction

Oncophage, our most advanced product candidate, is a personalized therapeutic cancer vaccine that is based on heat shock protein gp96 and is currently in Phase 3 clinical trials for the treatment of renal cell carcinoma and metastatic melanoma. Each Oncophage vaccine is made from a patient s tumor tissue. After a surgeon removes a patient s tumor, a portion of that tumor tissue is frozen and shipped overnight to our manufacturing facility in Massachusetts. In our current Phase 3 trials, we generally require seven grams of tumor tissue to yield a sufficient amount of Oncophage for a typical course of treatment.

Using a proprietary manufacturing process that takes approximately eight to ten hours per individual patient lot, we isolate the heat shock protein peptide complexes, or HSPPCs, from the tumor tissue. Through this isolation process, the HSPPCs are extracted and purified from the tumor tissue, then formulated in sterile saline solution and packaged in standard single injection vials. After the performance of stringent quality control testing, including sterility testing, we ship Oncophage frozen back to the hospital pharmacy for administration after a patient has fully recovered from surgery, which is usually four to six weeks later. A medical professional administers Oncophage by injecting the product into the skin weekly for four weeks and every other week thereafter until that patient s supply of Oncophage is depleted.