ANTIGENICS INC /DE/
Form 10-K405
March 28, 2002

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(D) OF

THE SECURITIES EXCHANGE ACT OF 1934

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2001 COMMISSION FILE NUMBER: 000-29089

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 No.)

630 FIFTH AVENUE, SUITE 2100,NEW YORK, NEW YORK 10111
(Address of principal executive offices including zip code)

REGISTRANT'S TELEPHONE NUMBER, INCLUDING AREA CODE: (212) 332-4774

SECURITIES REGISTERED PURSUANT TO SECTION 12(B) OF THE ACT:

NONE	NONE
(Title of each Class)	(Name of each exchange on which registered)

SECURITIES REGISTERED PURSUANT TO SECTION 12(G) OF THE ACT:
COMMON STOCK, $.01 PAR VALUE

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

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

The aggregate market value of voting stock held by non-affiliates of the registrant as of March 19, 2002 was: $295,564,618. There were 33,066,017 shares of the registrant's Common Stock outstanding as of March 19, 2002.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement of the registrant's 2002 Annual Meeting of Shareholders to be held on May 22, 2002, which definitive proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year of December 31, 2001, are incorporated by reference into Part III of this Annual Report on Form 10-K.

==========

This Annual Report on Form 10-K contains forward-looking statements, including statements regarding the timing of clinical trials, the safety and efficacy of our product candidates, our future research and development activities, estimates of the potential markets for our products, estimates of the capacity of manufacturing and other facilities to support our products, our expected future revenues, operations and expenditures, the timing of sales, and projected cash needs. These statements are subject to risks and uncertainties that could cause our actual results to differ materially from those that are projected in these forward-looking statements. These risks and uncertainties include, among others:

- our ability to successfully complete pre-clinical and clinical development of our products, which includes enrolling sufficient patients in our clinical trials and demonstrating the safety and efficacy of our product candidates in such trials;

- our ability to manufacture sufficient amounts of our products for clinical trials and commercialization activities;

- our ability to obtain, maintain and successfully enforce adequate patent and other proprietary rights protection of our products;

- the content and timing of submissions to and decisions made by the FDA and other regulatory agencies, including demonstrating to the satisfaction of the FDA the safety and efficacy of our product candidates;

- our ability to develop a sales and marketing staff and the success of their selling efforts;

- the accuracy of our estimates of the size and characteristics of the markets to be addressed by our products; and

- our ability to obtain reimbursement for our products from third-party payers, and the extent of such coverage.

We have included more detailed descriptions of these risks and uncertainties and other risks and uncertainties applicable to our business in Exhibit 99.1, "Risk Factors," to this Annual Report on Form 10-K. We encourage you to read those descriptions carefully. We caution investors not to place undue reliance on forward-looking statements contained in this document; such statements need to be evaluated in light of all the information contained in the document. Furthermore, the statements speak only as of the date of this document, and we undertake no obligation to update or revise these statements.

PART I

ITEM 1. BUSINESS

OUR BUSINESS

OVERVIEW

Through our core expertise in cancer, immunology and personalized medicine, we are focused on therapeutic vaccines and treatments for cancer, infectious diseases and autoimmune disorders. Our products are designed to improve on conventional treatments by prolonging survival, reducing side effects

and enhancing quality of life. Our lead development programs include immunotherapeutics that are based on a specific class of proteins known as heat shock proteins, also referred to as HSPs, and an immune system adjuvant called QS-21. In addition, we are developing Aroplatin and ATRA-IV, unique liposomal formulations of anticancer drugs that are designed to offer improvements over existing cancer drugs. Aroplatin and ATRA-IV fit our long-term goal of creating novel therapies for serious diseases that represent advanced alternatives to conventional cancer treatments.

OUR PRODUCTS UNDER DEVELOPMENT

INTRODUCTION

Through our internal discovery efforts and our recent acquisitions, we have developed a robust pipeline of products for the treatment of cancers and infectious diseases. Additionally, we have a receptor-based technology with which we intend to develop additional products, particularly in the fields of autoimmune disorders. Our lead product, Oncophage(R), uses our proprietary heat shock protein technology to stimulate a powerful T cell-based immune response capable of targeting and killing cancer cells. We believe that our HSP-based products will be able to treat all cancer types and several types of infectious diseases. We also believe that HSPs are applicable to the treatment of autoimmune disorders.

Oncophage is currently in Phase III trials in renal cell carcinoma and melanoma, and we intend to initiate an additional Phase III trial in melanoma in 2002. Oncophage is the first personalized therapeutic cancer vaccine to receive Fast Track designation from the U.S. Food and Drug Administration (FDA) and has received this designation in both renal cell carcinoma and in melanoma.

Aroplatin is a liposomal formulation of a novel platinum compound similar to oxaliplatin, a drug that is approved and marketed in Europe for the treatment of colorectal cancer. Aroplatin has been designed to overcome the resistance often associated with current platinum drugs as well as improve the side effect profile. We are developing Aroplatin in a variety of cancers and plan to initiate Phase II clinical trials of Aroplatin in colorectal and pancreatic cancers in 2002. We are also developing a clinical strategy to investigate Aroplatin in a Phase II trial in ovarian cancer in 2002.

ATRA-IV is a liposomal, intravenous formulation of all-trans-retinoic acid or ATRA. ATRA is approved and marketed in an oral formulation for the treatment of acute promyelocytic leukemia. Our

liposomal formulation of ATRA-IV is designed to increase its bioavailability. We are developing a clinical strategy to investigate ATRA-IV in a Phase II trial in one or more hematological malignancies in 2002.

AG-702 is our heat shock protein based therapy for genital herpes. Early studies in animals show that HSPs induce disease-specific T-cell-mediated immune responses. We initiated a Phase I trial for AG-702 in the fourth quarter of 2001.

QS-21 is a natural product that is used as an adjuvant, or companion compound, in vaccines to significantly improve the quality of immune response. QS-21 is used in products being developed by several pharmaceutical and biotechnology companies for the treatment of several chronic and debilitating diseases including malaria, hepatitis B, melanoma and HIV. FeLV/QA-21, our feline leukemia product, is a recombinant subunit vaccine that uses an immune stimulant in the same family as QS-21 and is marketed outside the U.S.

Through our discovery research programs, we intend to develop additional novel compounds that are designed to be efficacious and less toxic than conventional therapy. Our lead discovery program is focused on the CD91 receptor, the pathway through which heat shock proteins activate cellular immune response. As a therapeutic target, the CD91 receptor may present a unique opportunity for controlling human immune response. The CD91 receptor may be relevant in shutting down the inappropriate immune response of autoimmune diseases such as diabetes, arthritis and multiple sclerosis. We have another discovery program involving the study of the CD1 receptor and related proteins involved in lipid-antigen presentation pathways. CD1 proteins have been identified as playing important roles in regulating immunity to certain infectious diseases, cancers and autoimmune disorders.

PRODUCT DEVELOPMENT PORTFOLIO

Below is a list of our product candidates under development.

PRODUCT	STATUS			
	MARKET	PHASE III	PHASE II	PHASE I
Oncophage		Kidney cancer Melanoma	Colorectal cancer Gastric cancer Non-Hodgkin's lymphoma	Pancreatic cancer
Aroplatin			Colorectal cancer(1) Pancreatic cancer(1)	
ATRA-IV			Hematological Malignancies(1)	

AG-702				Genital her
QS-21 Adjuvant(2)		Melanoma	HIV Malaria Hepatitis B Breast Cancer	S. pneumoni Tuberculosi Respiratory Virus

CD91	
CD1	
FeLV/QA-21(veterinary vaccine)	Feline leukemia

(1) Trials to begin in 2002
(2) All partnered programs with the exception of S. pneumonia

ONCOPHAGE

INTRODUCTION

Oncophage is our lead cancer product based on our pioneering work that demonstrated that HSPs activate T-cells. Oncophage consists of two components: (i) a variable component, consisting of fragments of proteins called peptides, which are necessary for the specific targeting of diseased cells and (ii) a constant component, consisting of a heat shock protein that activates the targeted T-cell-based immune response.

Heat shock proteins are present in all cells of all organisms from bacteria to mammals, and their structure and function are similar across these diverse life forms. Heat shock proteins are a class of proteins that play a major role in transporting peptides, including antigenic peptides, within a cell and are thus often called chaperones. In this capacity, heat shock proteins bind to the broad antigenic repertoire or fingerprint of the cell in which they reside.

The ability of heat shock proteins to chaperone peptides is key to our technology and to Oncophage. When we purify heat shock proteins from tumor cells or pathogen-infected cells, the heat shock proteins remain bound to the broad repertoire of peptides produced by the tumor or pathogen. When these purified heat shock protein-peptide complexes are injected into the skin, they stimulate a powerful T-cell-based immune response capable of targeting and killing the cancer cells or infected cells from which these complexes were derived. These purified heat shock protein-peptide complexes are the active component of Oncophage.

We are evaluating Oncophage in six different cancers in eight separate clinical trials. Because cancer is a highly variable disease from one patient to another, we purify from each patient's tumor tissue heat shock proteins that are bound, or complexed, to peptides specific to each patient's cancer. Each Oncophage cancer product is therefore a personalized product. After a surgeon removes a patient's tumor, the hospital or clinic ships a frozen portion of the tumor tissue by overnight courier to our facility. Depending on the dose, we require a minimum of one to five grams of tumor tissue to yield a sufficient amount of Oncophage for a typical course of treatment.

We formulate Oncophage in sterile saline solution and package it in standard single injection vials in our manufacturing facility. We subject the final product to extensive quality control testing, including sterility testing of each lot. We ship the product frozen via overnight courier back to the hospital.

We have developed sophisticated tracking systems and procedures designed to ensure correct delivery of Oncophage to the appropriate patient.

A medical professional initially administers Oncophage to a patient four to six weeks after a doctor surgically removes the patient's primary or metastatic tumor. The typical course of treatment consists of an injection into the skin administered once per week for four weeks and every other week thereafter. An oncologist may recommend treating a patient with more than one course of Oncophage.

Although we believe Oncophage will be able to treat all cancer types, our initial focus is on cancers that are resistant to available treatment and that typically yield tumors that physicians can surgically remove. Additionally, in order to complete clinical trials rapidly and file for regulatory approvals, we have selected cancers and stages of disease that allow us to evaluate Oncophage in clinical trials with near term endpoints.

We filed an IND for Oncophage in November 1996 that the FDA allowed on December 20, 1996. We started enrolling patients in our first clinical trial at Memorial Sloan-Kettering Cancer Center in New York, New York in November 1997. To date, we have treated over 300 cancer patients with Oncophage in our clinical trials.

We believe that the collective results from these clinical trials show that Oncophage is generally safe and well tolerated by patients with little side effects. We also believe that these results demonstrate that treatment with Oncophage can generate immunological and anti-tumor responses and prolong survival.

ONCOPHAGE CLINICAL PROGRAMS

RENAL CELL CARCINOMA

BACKGROUND. Renal cell carcinoma is the most common type of kidney cancer. The American Cancer Society estimates that physicians will diagnose about 31,800 new cases of kidney cancer in the United States in 2002 and that the disease will kill approximately 11,600 people in 2002. Approximately 70% of the 31,800 patients newly diagnosed with kidney cancer will have the specific type of kidney cancer known as renal cell carcinoma. By the time renal cell carcinoma is diagnosed in these patients, about one-third of them will have developed metastatic disease.

The median survival of patients with metastatic renal cell carcinoma is approximately 12 months. For patients with metastatic disease, the only FDA approved treatment is intravenous high-dose interleukin-2, a human cytokine. The response rate, which includes partial responses and complete responses, of patients who are treated with high-dose interleukin-2 is approximately 15%. Treatment with high-dose interleukin-2 often causes severe adverse side effects. These side effects often can lead to discontinuation of treatment. Although not FDA-approved for the treatment of renal cell carcinoma, a lower-dose of interleukin-2 injected underneath the skin, or subcutaneously, either alone or in combination with other cytokines, has become a treatment option. This treatment regimen has been the subject of a number of studies with widely varying outcomes, none of which have demonstrated any survival benefit.

CLINICAL TRIALS. In a Phase I/II trial, we enrolled patients with measurable metastatic renal cell carcinoma. Of the 34 evaluable patients, 13 patients responded or had stable disease. Four patients had a partial response, and one patient had a minor response. The other eight patients showed stabilization of

their disease. Three of these patients had been stable for more than 10 months at the time the trial was concluded. The response rate in this trial, which does not include patients with a minor response or stable disease, was 12% and no serious adverse events were associated with treatment with Oncophage. The median survival in this trial is 13 months.

A 60 patient Phase II trial for patients with metastatic renal cell carcinoma was initiated at M.D. Anderson Cancer Center in March 1999. In an interim analysis of the Phase II study, 35% of the patients treated with Oncophage alone showed an improvement in the course of the disease. Oncophage received Fast Track designation for the treatment of renal cell carcinoma in October 2001. Oncophage is the first personalized cancer vaccine to receive Fast Track designation. In 2001, we initiated a Phase III, multicenter, international trial for renal cell carcinoma in which we have now enrolled 150 patients.

MELANOMA

BACKGROUND. Melanoma is the most serious form of skin cancer. The American Cancer Society estimates that physicians will diagnose about 53,600 new cases of melanoma in the United States in 2002 and that the disease will kill approximately 7,400 people in 2002. The incidence of melanoma is growing at a rate of 4-7% per year, which is substantially faster than the growth in incidence rates of most other cancers. Oncologists treat advanced or metastatic melanoma, also known as stage III or IV, with surgery, radiation therapy, immunotherapy, or chemotherapy depending on the case. Approximately 20% of all melanoma patients at the time of their first diagnosis have stage III or stage IV disease. Existing treatments have not significantly improved overall survival of patients with melanoma. The median survival of patients with stage III melanoma varies widely according to published literature. According to published literature, the median survival of patients with late stage III melanoma is 24 months and patients with stage IV melanoma have a median survival of about seven months. Although oncologists use various treatments, the only FDA approved therapies for patients with metastatic melanoma are high-dose intravenous interleukin-2 and alpha interferon, another human cytokine.

CLINICAL TRIALS. We have treated 36 patients in a Phase I/II clinical trial, evaluating Oncophage as a treatment for late stage III and early stage IV metastatic melanoma, as well as 28 patients in a Phase II clinical trial in patients with stage IV disease. In the Phase II trial, five patients responded favorably to Oncophage including two in whom all evidence of melanoma disappeared for more than two years. Oncophage vaccination also generated anti-melanoma immune response in more than one-half of the patients. We presented the results of the Phase II trial both at the American Society of Clinical Oncology (ASCO) meeting in May 2001 and the American Association for Cancer Research (AACR) meeting in

October 2001 where it was selected by the conference organizers as one of six presentations out of over 800 to be highlighted and presented to the press. In February 2002, Oncophage received Fast Track designation for the treatment of metastatic melanoma.

We initiated a Phase III trial in metastatic melanoma in February 2002, and are in the final stages of trial design for a second Phase III trial in melanoma planned to start later in 2002.

OTHER CANCERS

COLORECTAL. We have completed enrollment of a 30 patient Phase II clinical trial evaluating Oncophage as a treatment for metastatic colorectal cancer. Interim

data from 29 patients with advanced colon cancer that had spread to the liver indicates that Oncophage therapy generated anti-colon cancer immune response in close to half of the patients. Although the study was not designed to evaluate clinical effectiveness, a small group of patients with favorable prognostic factors who received Oncophage were cancer-free longer than expected. This data will be available in an abstract at the ASCO meeting in 2002.

GASTRIC. We completed enrollment of a 30 patient Phase I/II clinical trial evaluating Oncophage as a treatment for metastatic gastric cancer. We conducted this trial with clinical investigators at the Johannes Gutenberg-University Hospital in Mainz, Germany, Technical University of Munich in Germany, and the Russian Oncology Research Center in Moscow, Russia. We will be presenting data from this trial at the ASCO meeting in 2002.

PANCREATIC. In early 1999, we completed a pilot Phase I clinical trial evaluating Oncophage as a treatment for resectable pancreatic cancer. We conducted the trial with clinical investigators at the Memorial Sloan-Kettering Cancer Center and enrolled 15 patients. The clinical investigators treated five of the 15 patients with five micrograms of Oncophage after physicians had removed each patient's primary tumor. Two out of five patients generated a T-cell response to their tumor after treatment with Oncophage. We successfully prepared Oncophage from five of 15 pancreatic cancer samples we received in our manufacturing facility. We were not able to prepare Oncophage from the remaining tumor samples due to the presence of enzymes in the pancreatic tissue that break down proteins, including heat shock proteins. Since improving our manufacturing process for pancreatic cancer, we have successfully produced vaccine from six of eight additional patients, one of whom was not treated because of other exclusion criteria. The remaining two patient batches were unsuccessful due to the miniscule size of the tumor (