ALFACELL CORP
Form 10-K
October 14, 2004

U. S. SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

July 31, 2004	0-11088
For the fiscal year ended	Commission file number

ALFACELL CORPORATION
(Exact name of registrant as specified in its charter)

Delaware	22-2369085
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

225 Belleville Avenue, Bloomfield, New Jersey 07003
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (973) 748-8082

Securities registered pursuant to Section 12(b) of the Act: None

Securities registered pursuant to Section 12(g) of the Act:

Common Stock, $.001 par value
(Title of Class)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes |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 any amendment to this Form 10-K. |_|

Indicate by check mark whether the registrant is an accelerated filer (as defined in Exchange Act Rule 12b-2). Yes |X| No |_|

The aggregate market value of the common stock, par value $.001 per share, held by non-affiliates based upon the reported last sale price of the Common Stock on January 31, 2004 was approximately $128,365,000. As of October 8, 2004 there were 34,980,314 shares of common stock, par value $.001 per share, outstanding.

Documents Incorporated by Reference

Portions of the registrant's definitive Proxy Statement for the Annual Meeting of the Stockholders scheduled to be held on January 27, 2005, to be filed with the Commission not later than 120 days after the close of the registrant's fiscal year, have been incorporated by reference, in whole or in part, into Part III Items 10, 11, 12, 13 and 14 of this Annual Report on Form 10-K.

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The following trademarks appear in this Annual Report: ONCONASE(R) is the registered trademark of Alfacell Corporation, exclusively for the anti-cancer indications; Alimta(R) and Gemzar(R) are registered trademarks of Eli Lilly; Navelbine(R) is a registered trademark of Glaxo Smith Kline.

All information on this Form 10-K is as of October 14, 2004 and we undertake no obligation to update this information.

We maintain a website at www.alfacell.com to provide information to the general public and our stockholders on our products, resources and services along with general information on Alfacell, its management, financial results and press releases. Copies of our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q or our other reports filed with the Securities and Exchange Commission, or SEC, can be obtained, free of charge as soon as reasonably practicable after such material is electronically filed with, or furnished to the SEC, from our Investor Relations Department by calling 973-748-8082, through an e-mail request from our website at www.alfacell.com/info.htm, or through the SEC's website by clicking the direct link from our website at www.alfacell.com/investinfo.htm or directly from the SEC's website at www.sec.gov. Our website and the information contained therein or connected thereto are not intended to be incorporated into this Annual Report on Form 10-K.

Our Board of Directors has adopted a Code of Business Conduct that is applicable to all of our directors, officers and employees. Any material changes made to our Code of Business Conduct or any waivers granted to any of our directors and executive officers will be publicly disclosed by filing a current report on Form 8-K within five business days of such material change or waiver. We intend to make the Code of Business Conduct available on our website at www.alfacell.com. Although our Board of Directors has not established a nominating committee, our formal nominating procedures will be described in our definitive proxy statement for the Annual Meeting of Stockholders to be held on January 27, 2005. In addition, copies of such documents are available to our shareholders upon request either by contacting our Investor Relations Department at 973-748-8082 or through an e-mail request from our website at www.alfacell.com/info.htm.

Information contained herein contains, in addition to historical information, forward-looking statements that involve risks and uncertainties. All statements, other than statements of historical fact, regarding our financial position, potential, business strategy, plans and objectives for future operations are "forward-looking statements." These statements are commonly identified by the use of forward-looking terms and phrases such as "anticipates," "believes," "estimates," "expects," "intends," "may," "seeks," "should," or "will" or the negative thereof or other variations thereon or comparable terminology, or by discussions of strategy. Actual future results may vary from expectations set forth in these forward-looking statements. The matters set forth herein under the caption "Risk Factors" constitute cautionary statements identifying important factors with respect to these forward-looking statements, including certain risks and uncertainties, that could cause actual results to vary significantly from the future results indicated in these forward-looking statements. Other factors could also cause actual results to differ significantly from the future results indicated in these forward-looking statements.

Part I

Item 1. BUSINESS.

Overview

Alfacell Corporation is a biopharmaceutical company primarily engaged in the discovery and development of a new class of therapeutic drugs for the treatment of cancer and other pathological conditions. Based on our proprietary Ribonuclease, or RNase, which is a type of biological enzyme that splits RNA molecules and is the basis of our technology platform, our drug discovery and development program consists of novel therapeutics developed from amphibian ribonucleases. These are very basic RNA enzymes which play important roles in nature in the development of an organism's cells and in cell functions. RNA is an essential bio-chemical cellular component necessary to support life. There

are various types of RNA, all of which have specific functions in a living cell. They help control several essential biological activities, namely, regulation of cell proliferation, maturation, differentiation and cell death. Therefore, they are ideal candidates for the development of therapeutics for cancer and other life-threatening diseases, including HIV and autoimmune diseases, that require anti-proliferative and apoptotic, or programmed cell death, properties. We have co-sponsored and been a key participant in the International Ribonuclease Meetings which are held every three years.

ONCONASE(R), our trademark name for our lead product, is currently in an international, centrally randomized Phase III trial. The first part of the trial has been completed and the second confirmatory part of the trial is ongoing for which patient enrollment is expected to be completed in the first quarter of 2005. The primary endpoint of the trial is survival, and as such, a sufficient number of deaths must occur in order to perform the

required statistical analyses to determine the efficacy of ONCONASE(R) in patients with unresectable (inoperable) malignant mesothelioma. If the results of the clinical trials are positive, we expect to file for marketing registrations (NDA and MAA) for ONCONASE(R) within six months of completion of the statistical analyses. However, at this time, we cannot predict with certainty when a sufficient number of deaths will occur to achieve statistical significance. Hence, the timing of when we will be able to file for marketing registrations in the US and EU is data driven. Therefore, we cannot predict with certainty what our total cost associated with obtaining marketing approvals will be, or when and if such approvals will be granted, or when actual sales will occur. We have also conducted other randomized and non-randomized trials with patients with advanced stages of solid tumors in other types of cancers.

ONCONASE(R), unlike most cancer drugs that attack all cells regardless of their phenotype, malignant versus normal, and produce a variety of severe toxicities, is not an indiscriminate cytotoxic, or cell killing agent, but rather, its activity is controlled through unique and specific molecular mechanisms. ONCONASE(R) affects primarily exponentially growing malignant cells. ONCONASE(R) is a novel amphibian ribonuclease, unique among the superfamily of pancreatic ribonuclease that has been isolated from the eggs of the Rana pipiens frog, commonly called the leopard frog. We have determined that, thus far, ranpirnase, the generic name of ONCONASE(R), is the smallest known protein belonging to the superfamily of pancreatic ribonuclease and has been shown, on a molecular level, to re-regulate the unregulated growth and proliferation of cancer cells.

In December 2002, we received Fast Track Designation from the FDA for ONCONASE(R) for the treatment of malignant mesothelioma. Fast Track Designation is an FDA program designed to expedite the review of new drugs that are intended to treat serious or life threatening conditions and that demonstrate the potential to address unmet medical needs. In February 2001, we received an Orphan Medicinal Product Designation for ONCONASE(R) from the European Agency for the Evaluation of Medicinal Products, or the EMEA. Orphan Medicinal Product Designation is a program designed to provide marketing, protocol and other incentives for pharmaceutical companies to develop and market products in the European Community that address life threatening or very serious conditions that affect not more than 5 in 10,000 persons in the European Community. Orphan designation in Europe entitles the Company to 10 years of marketing exclusivity, reduced filing fees and regulatory guidance from the EMEA.

These FDA and EMEA designations for ONCONASE(R) may serve to expedite its regulatory review, assuming the clinical trials yield a positive result. Future

clinical trials, however, may not demonstrate that ONCONASE(R) is effective. Thus, our applications for FDA or EMEA approval to market ONCONASE(R), which are dependent upon the success of our clinical trials, may be affected. The efficacy and safety of ONCONASE(R) for malignant mesothelioma will ultimately be determined by the FDA. In the interim, our Fast Track Designation allows us to continue to have meetings and discussions with the FDA to establish mutually agreed upon parameters for the NDA to obtain marketing approval for ONCONASE(R), based on the assumption that the clinical trials will continue to yield favorable results.

Our drug discovery program forms the basis for the development of specific recombinant RNases for chemically linking drugs and other compounds such as monoclonal antibodies, growth factors, etc. and gene fusion products with the goal of targeting various molecular functions. This program provides for joint design and generation of new products with outside partners. We may own these new products along with a partner(s), or we may grant an exclusive license to the collaborating partner(s).

We have established a number of scientific collaborations with academic and research institutions including the National Cancer Institute, or NCI that are designed to develop new therapeutic applications for ONCONASE(R). One collaboration has produced RN321, a conjugate of ranpirnase, with a monoclonal antibody that demonstrated activity in treating non-Hodgkin's lymphoma in preclinical studies. These results were presented by the NCI investigators at the 2002 Ribonuclease Meeting in Bath, England. The NCI has undertaken the manufacturing of RN321 (the conjugate) according to Good Manufacturing Practices, or GMP regulations in preparation for commencing clinical trials for the treatment of patients with non-Hodgkin's lymphoma with RN321. Currently, the NIH has produced RN321 clinical grade like material. Clinical grade production of RN321 and Investigational New Drug Application, or IND, directed toxicology studies will require further approval from the Drug Development Group of the NIH prior to commencing human clinical trials.

We have also discovered another series of proteins, collectively named amphinases that may have therapeutic uses. These proteins are bioactive in that they have an effect on living cells and organisms and have both anti-cancer and anti-viral activity. All of the proteins characterized to date are RNases. These products are currently undergoing preclinical testing. We are currently in discussions with potential pharmaceutical partners for the development of these new compounds as conjugates and fusion proteins.

We have entered into a research and development collaboration with a major US privately held stent and drug delivery company. ONCONASE(R) is being evaluated in stents and other delivery platforms to treat cardiovascular disease and cancer via direct site delivery. This collaboration may result in licensing agreement between the companies, however; there is no assurance that such agreement will be reached.

We have entered into a collaborative agreement (anti-viral screening, non-SARS) with the National Institute of Allergy and Infectious Diseases, or NIAID in which five potential drug candidates (natural and genetically engineered) are under evaluation against various RNA viruses.

Our research and development collaboration with Wyeth Pharmaceuticals is ongoing to develop a number of designer drugs such as conjugates and fusion proteins for a variety of indications using our technology. This collaboration may result in a licensing agreement between the companies, however; there is no assurance that such an agreement will be reached.

We have signed confidentiality agreements and have entered into discussions and due diligence with a number of companies for US or non-US marketing rights for ONCONASE(R) and for out-licensing some of our early drug candidates.

We are engaged in the research, development and clinical trials of our products both independently and through research collaborations. We have financed our operations since inception through the sale of our equity securities and convertible debentures in registered offerings and private placements. Additionally, we have raised capital through debt financings, the sale of our tax benefits and research products, interest income and financing received from our Chief Executive Officer. These funds provide us with the resources to acquire staff, facilities, capital equipment, finance our technology, product development, manufacturing and clinical trials. We have incurred losses since inception and to date we have not consummated any licensing, marketing or development arrangements. Presently, our cash balance is sufficient to fund our expanded operations through October 31, 2005 based on our expected level of expenditures in relation to activities in preparing ONCONASE(R) for an NDA filing and other ongoing operations of the company. However, we continue to seek additional capital financing through the sale of equity in private placements, sale of our tax benefits and exercise of stock options and warrants but cannot be sure that we will be able to raise capital on favorable terms or at all.

Research and Development Programs

Research and development expenses for the fiscal years ended July 31, 2004, 2003, and 2002 were $3,353,000, $1,700,000, and $2,033,000, respectively. Our research and development programs focus primarily on the development of therapeutics from amphibian ribonucleases. Because ribonucleases have been shown to be involved in the regulation of cell proliferation, maturation, differentiation and programmed cell death, known as apoptosis, ribonucleases may be ideal candidates for the development of therapeutics for the treatment of cancer and other life-threatening diseases, including viral and autoimmune diseases that require anti-proliferative and pro-apoptotic properties.

Technology Platform and Pipeline

Using ribonucleases as therapeutics is a relatively new approach to drug development. The use of these proteins to re-regulate the unregulated growth and proliferation of cancer cells is unlike most cancer drugs that attack all cells regardless of their phenotype, malignant versus normal, and produce a variety of severe toxicities.

ONCONASE(R) and related drug candidates are not indiscriminate cytotoxic, or cell killing, agents, but rather, their activity is controlled through unique and specific molecular mechanisms. They affect primarily exponentially growing malignant cells.

Cancer is associated with the over or under production of many types of proteins in tumor cells. We believe that the ability to selectively halt the production of certain proteins via ribonuclease activity in tumor cells without damaging normal cells, may make treatment of cancer more effective. To make cancer therapy more effective and less toxic, we are developing ONCONASE(R) and a related family of regulatory proteins, collectively named amphinases. These novel RNases are being developed as therapeutics as well as effector moieties (payload), or killer molecules for targeted therapies. We believe that selective

degradation of intracellular proteins is central to the process of programmed cell death.

We have devoted significant resources towards the development of recombinant designer RNases for chemical conjugation and gene fusion products with various targeting moieties such as monoclonal antibodies, growth factors, cytokines, etc.

Apoptosis

Apoptosis, or programmed cell death, is essential for the proper development of embryos and of many body systems, including the central nervous system, immune regulation and others. Apoptosis is required to accommodate the billions of new cells produced daily by our bodies and to eliminate aged or damaged cells. Abnormal regulation of the apoptosis process can result in disease. For example, cancer, autoimmune disorders and many viral infections are associated with inhibited apoptosis or programmed death of cells occurring too slowly. Conversely, HIV is associated with increased apoptosis or programmed death of cells occurring too rapidly. The process of programmed cell death is genetically regulated. We believe that we are the first company to discover and develop a novel family of primordial "regulatory" proteins that have been shown to play a fundamental role in this regulatory process.

ONCONASE(R) (ranpirnase) Pro-Apoptotic Mechanisms

The molecular mechanisms were identified which determine the apoptotic cell death induced by ranpirnase. tRNA, rRNA and mRNA are all different types of RNA with specific functions in a living cell. Ranpirnase preferentially degrades tRNA, leaving rRNA and mRNA apparently undamaged. The RNA damage induced by ranpirnase appears to represent a "death signal", or triggers a chain of molecular events culminating in the activation of proteolytic enzyme cascades which, in turn, induces disintegration of the cellular components and finally leads to cell death. It has been shown that there is a protein synthesis inhibition-independent component, which, together with the changes induced by the protein synthesis inhibition, results in tumor cell death.

Many cancer cells become resistant to most types of cancer treatment, including chemotherapy, radiation and monoclonal antibodies. Overcoming resistance to chemotherapy remains a major challenge for cancer therapy. ONCONASE(R) has been shown to overcome multiple drug resistance or prevent resistance to cancer therapy, thereby dramatically increasing the sensitivity of certain cancer cells to chemotherapy and radiation therapy.

It remains unknown whether or not ONCONASE(R) targets and binds preferentially to tumor cells, rather than normal cells of the respective tissues. It is possible that there is no differential targeting and/or binding, but that tumor cells are more susceptible to the cytostatic (suppresses cancer cells from further dividing) and cytotoxic (kills cancer cells) effects of ONCONASE(R). The cytostatic effects are manifested by the inhibition of progression in the cell cycle. These effects have been associated with induction of parallel differentiation and apoptosis. The cytostatic and differentiation-inducing effects are reflected in the stabilization of previously progressive tumors observed in our clinical trials.

Clinical Studies and Preclinical Development of ONCONASE(R)

We have been very selective in our product development strategy, which is focused on the use of ONCONASE(R) alone or in combination with drugs which have shown evidence of preclinical and clinical efficacy on

tumor types for which median survivals are typically less than a year and for which there are few or no approved treatments.

ONCONASE(R) has been tested in Phase I, Phase II and Phase III clinical trials in more than 40 cancer centers across the United States since 1991 and in Europe since 2000, including major centers such as Columbia-Presbyterian, University of Chicago, M.D. Anderson and Cedars-Sinai Cancer Centers.

ONCONASE(R) has been tested as a single agent in patients with a variety of solid tumors. It has also been tested in combination with tamoxifen in patients with prostate cancer, advanced pancreatic cancer and renal cell carcinoma as well as with doxorubicin in patients with malignant mesothelioma.

We have collaborated with NIH, NCI and The University of Pennsylvania Medical Center, Metabolic Magnetic Resonance Research and Computing Center, and have developed a considerable body of knowledge in RNase technology and novel RNase-based therapeutics. ONCONASE(R) has demonstrated a broad spectrum of anti-tumor activity in vitro, or studies of tumor cell lines in laboratory vessels, and was determined to kill cancer cells and therefore was judged to be "active" in the NCI Cancer Screen.

In vitro and in vivo studies showed both cytostatic (suppresses cancer cells from further dividing) and cytotoxic (kills cancer cells) antitumor activity when used as a single agent and in combination with other agents.

In Vitro

ONCONASE(R), in combination with other drugs has been shown to be synergistic, which means that the effect of ONCONASE(R) when given in combination with other drugs is greater than if the drugs were given alone. The combination of ONCONASE(R) and tamoxifen, an anti-cancer drug, resulted in a significant cell kill in pancreatic, prostate, and ovarian tumor cell lines as compared to each drug alone. Similar results were found with respect to the following:

- ONCONASE(R) + phenothiazine for non-small cell lung cancer;
- ONCONASE(R) + lovastatin in pancreatic, ovarian, and two types of non-small cell lung cancer;
- ONCONASE(R) + cisplatin in ovarian cancer;
- ONCONASE(R) + all-trans-retinoic acid in glioma (brain) cancer;
- ONCONASE(R) + vincristine in colorectal cancer and ;
- ONCONASE(R) + doxorubicin in breast cancer including resistant variants, malignant mesothelioma.

In Vivo Anti-Cancer Activity

ONCONASE(R) as a Single Agent

ONCONASE(R), as a single agent has shown in vivo anti-tumor activity in several mouse models of solid tumors. The following are all examples of the effect of ONCONASE(R) on various types of human cancer cells in mouse models:

- In the human squamous A-253 carcinoma and the NIH-OVCAR-3 ovarian adenocarcinoma models, ONCONASE(R) has produced prolonged survival and delayed time to development of ascites (fluid in the abdomen),

respectively.

- In mice bearing M109 Madison lung carcinoma cells, time to appearance of ascites and survival were significantly prolonged in ONCONASE(R) treated animals as compared to controls. Several histologically (microscopic study of cells) confirmed cures were noted.

- In nude mice bearing human DU-145 prostate carcinoma and pancreatic ASPC-1 carcinoma, ONCONASE(R) inhibited growth of the subcutaneously transplanted tumor.

- In several mouse tumor models, ONCONASE(R) not only demonstrated direct anti-tumor activity but also increased the potential for other drugs to penetrate the tumor tissue as well as increased the tumor sensitivity to radiation therapy.

ONCONASE(R) in Combination With Other Agents

Based on in vivo results, ONCONASE(R) in combination with the following known and approved anti-cancer agents has been evaluated by us, in collaboration with the NCI:

- vincristine

- doxorubicin

- tamoxifen

When used in combination with vincristine, ONCONASE(R) prolonged the survival of nude mice bearing vincristine-resistant, HT-29 human colorectal carcinomas, a type of cancer cell, transfected with mdr-1 gene, a multiple drug resistant gene. These NCI results demonstrated that ONCONASE(R) can restore the sensitivity of resistant tumor cells to chemotherapy.

NCI experiments in nude mice transplanted intravenously with human breast carcinoma cells treated with the combination of ONCONASE(R) and doxorubicin have shown significantly prolonged survival. Tumor growth was significantly inhibited as demonstrated by a decrease in the number of pulmonary metastases, or disseminated lesions in the lung, present at the time of sacrifice.

NCI reported the ability of ONCONASE(R) to overcome multiple drug resistance as well as other forms of drug resistance (referring to a drug that no longer kills cancer cells) both in vitro and in vivo. We believe that these in vivo results demonstrate the therapeutic utility of ONCONASE(R) in chemotherapy-resistant tumors, and the findings suggest that ONCONASE(R) in combination with other agents has broad clinical application in cancer treatments.

Clinical Trials

Onconase(R) Phase III Randomized Clinical Trials

We are currently conducting a two-part Phase III clinical trial of ONCONASE(R) as a treatment for malignant mesothelioma. The first part of the Phase III trial compares ONCONASE(R) alone to doxorubicin. Doxorubicin has been considered by opinion leaders to be the most effective drug for the treatment of malignant mesothelioma. The second part of the trial compares the combination of

ONCONASE(R) and doxorubicin versus doxorubicin alone. The trial is an open label, centrally randomized, controlled study. The patient enrollment for the first part of the clinical trial has been completed and the trial is on-going. The second part is currently in the enrollment stage and is being conducted in the United States, Europe, Canada and Australia.

Since ONCONASE(R) has Fast Track Designation for the treatment of malignant mesothelioma patients, we continue to have meetings and discussions with the FDA to establish mutually agreed upon parameters for the New Drug Application, or NDA, to obtain marketing approval for ONCONASE(R), assuming the Phase III clinical trial yields favorable results.

Phase III Single Agent Results

An interim subset analysis of the results of this Phase III clinical trial according to the Cancer Adult Leukemia Group B, or CALGB, prognostic groups revealed a marked excess of poor prognosis patients (groups 5 and 6) in the ONCONASE(R) arm of the trial (32 patients or 38.1% of the patients treated with ONCONASE(R)) as compared to the doxorubicin arm of the trial (12 patients or 17% of the patients treated with doxorubicin). By excluding these patients and the 10 patients whose central pathology review did not confirm a diagnosis of malignant mesothelioma (N=5) from the 154 intent-to-treat patients, we defined a target treatment group, or TTG, consisting of 104 patients who met the criteria for CALGB prognostic groups 1-4. Of these patients, 47 were treated with ONCONASE(R) and 57 were treated with doxorubicin. The single agent Phase III results of the TTG showed a median survival benefit, or MST, of 2 months for ONCONASE(R) treated patients, 11.6 months versus 9.6 months.

This two month median survival difference favoring ONCONASE(R) represents a 20% advantage over the active agent, doxorubicin. Moreover, the clinical activity of ONCONASE(R) is also evident from the overall 1-year and 2-year survival rates of ONCONASE(R) versus doxorubicin, 46.8% versus 38.6% and 20.2% versus 12.3%, respectively. Doxorubicin treatment was associated with a 60% higher risk of death compared to ONCONASE(R) treatment. Tumor assessment by an independent radiologist for evaluable patients (had a baseline and follow-up radiological assessment) revealed evidence of objective clinical activity in 17 patients in each treatment arm. Four partial responses and 13 stabilization of previously progressive disease were reported in the ONCONASE(R) treated patients and 7 partial responses and 10 stabilization of previously progressive disease were reported in the doxorubicin treated patients. Despite the small number of patients, the analysis revealed a statistically significant difference, log rank test, p. = 0.037, in survival of the responders favoring ONCONASE(R) treated patients with an MST 23.3 versus 14.4 months for doxorubicin treated patients as well as the 2 year survival rates of 40% for ONCONASE(R) and 9% for doxorubicin. Preliminary results were presented at the 2000 American Society of Clinical Oncologists, or ASCO, meeting.

These survival advantages were recognized as clinically important in this patient population by opinion leaders and the FDA. Therefore, the FDA has requested confirmation of the survival results in the TTG population in the second part of the ongoing trial.

In December 2002, we received Fast Track Designation from the FDA for ONCONASE(R) and doxorubicin for the treatment of malignant mesothelioma. Fast Track is a formal mechanism to interact with the FDA using approaches that are available to all applicants for marketing claims for drugs that are being developed for a serious or life-threatening disease for which there is an unmet medical need. The benefits of Fast Track include scheduled meetings to seek FDA

input into development plans, the option of submitting an NDA in sections rather than all components simultaneously, and the option of requesting evaluation of studies using surrogate endpoints. We anticipate to use this designation to reduce the marketing approval timeline for ONCONASE(R).

In February 2001, we received an Orphan Medicinal Product Designation for ONCONASE(R) from the European Agency for the Evaluation of Medicinal Products, or the EMEA. Orphan Medicinal Product Designation is a program designed to provide marketing, protocol and other incentives for pharmaceutical companies to develop and market products in the European Community that address life threatening or very serious conditions that affect not more than 5 in 10,000 persons in the European Community. Orphan designation in Europe entitles the Company to 10 years of marketing exclusivity, reduced filing fees and regulatory guidance from the EMEA. We continue to fulfill the EMEA requirements regarding the Marketing Authorization Application, or MAA registration requirements for ONCONASE(R) for the treatment of malignant mesothelioma.

In part two of the ongoing Phase III trial, interim analyses based on the occurrence of 105 deaths and at 210 deaths are planned. Based upon the results of these analyses, we may be able to file an NDA and an MAA within six months after the completion of the analyses. However, we cannot assure you that marketing approval for ONCONASE(R) as a treatment for malignant mesothelioma will be granted by the FDA or EMEA.

Based on Phase II trial results after meeting with the FDA, we had initiated a Phase III trial in patients with advanced pancreatic cancer in 1995. In the Phase II trial, the median survival time of 5.5 months for 47 patients with stage 4 disease and liver involvement treated with the combination of ONCONASE(R) weekly and tamoxifen daily was more than double the median survival of such patients reported in previously published trials treated with a variety of other systemic therapies (published median survival times ranged from 2.0 to 2.5 months). The Phase III trial was a multicenter randomized trial designed to evaluate an ONCONASE(R) and tamoxifen regimen in untreated patients as well as patients who had failed GEMZAR(R), an approved drug for pancreatic cancer. The primary endpoint of both segments of this Phase III trial was survival, however, early survival analyses of both segments did not reveal a significant survival advantage of ONCONASE(R) over the controls. Thus, due to the negative results of the Phase III trial, despite favorable results produced in Phase II, competitive pressures and our inability to accrue qualified patients in the clinical trials, we made a decision that further evaluation of this end-stage patient population was not warranted at that time and our resources were refocused on the ongoing malignant mesothelioma program.

ONCONASE(R) Phase II Clinical Trials

ONCONASE(R) as a single agent, demonstrated objective clinical activity in 105 patients with uresectable, or inoperable, malignant mesothelioma that included many heavily pretreated patients with refractory tumors, which are tumors that did not readily yield to the treatment. Analysis of the TTG population confirmed the importance of the CALGB prognostic groups and their utility for evaluating systemic therapies in this patient population.

Of the 105 patients treated, 41 patients, or 39%, reported evidence of clinical activity. Of the patients showing evidence of clinical activity, there were four with partial responses, two with minor responses and 35 showed evidence of stabilization of previously progressive disease. The MST of these patients was 18.5 months and the overall 1-year and 2-year survival rates were 61% and 40.8%, respectively. The results of this trial demonstrated a survival

benefit for both newly diagnosed patients and patients who failed prior therapies. The presentation of this data to the FDA resulted in the design of our Phase III malignant mesothelioma trial.

A multicenter Phase II Broad Eligibility trial designed to evaluate ONCONASE(R) as a single agent has been conducted and results of the findings for patients with non-small cell lung cancer, or NSCLC, and advanced breast cancer were published.

ONCONASE(R) as a single agent, demonstrated objective clinical activity in patients with advanced NSCLC and breast cancer. The median survival time of 30 patients with advanced NSCLC was greater than that in 19 of 20 regimens when supportive care, a placebo or another single agent was given. Furthermore it was greater than 75% of the reported MSTs in combination chemotherapy trials. The MST and 1 year survival rates of 7.7 months and 27%, respectively, for ONCONASE(R) treated patients compared favorably to 7.2 months and 30% for patients treated with Navelbine(R) (an approved drug for this indication) as a single agent.

Thirty percent of 17 patients with advanced breast cancer demonstrated objective clinical activity, which included, one partial response, two minor responses, the significant reduction in bone pain in one patient, and the control of uncontrollable malignant fluid in the lungs of another patient.

A series of pilot Phase II studies to evaluate ONCONASE(R) as a single agent, and ONCONASE(R) and tamoxifen in previously treated patients with unresectable, or inoperable, renal cell cancer were conducted. The results of both the Phase II single agent and ONCONASE(R) and tamoxifen were published. Although the single agent study did not demonstrate evidence of clinical activity, the regimen of ONCONASE(R) and tamoxifen did demonstrate evidence of clinical activity which indicated further evaluation in untreated patients was warranted.

Research And Development Pipeline Of Targeted Therapies

Our drug discovery program forms the basis for the development of recombinant designer RNases for chemical conjugation and gene fusion products with various targeting moieties such as monoclonal antibodies, growth factors, cytokines, etc. We believe these products can be produced in a cost effective and controlled manufacturing environment.

This program also provides for joint design and generation of new products with outside partners. We, along with any outside partners, may own these new products jointly, or we may grant an exclusive license to the collaborating partner(s).

Ranpirnase Conjugates and Fusion Proteins

The concept of targeting potent toxins as effector molecules to kill cancer or other specifically targeted cells has been extensively evaluated over the last two decades. An immunotoxin is an antibody linked to a toxic molecule that is used to destroy specific cells. Several immunotoxins containing bacterial and plant toxins or other biotoxins, have been evaluated in human clinical trials. Efficacy has always been limited due to the high incidence of immunogenicity, or an immune response, and other intolerable toxicities, including death. Conjugation of ranpirnase to targeting ligands, or binding to other molecules, appears to eliminate this safety problem in pre-clinical studies.

We have established a number of scientific collaborations with academic and research institutions including the NCI. The objective of our collaboration with the NCI is to develop new therapeutic applications for ONCONASE(R). This collaboration has produced RN321, a conjugate of ranpirnase, with a monoclonal antibody that demonstrated activity in treating non-Hodgkin's lymphoma in preclinical studies. The relative benefit in killing targeted tumor cells versus non-targeted healthy cells, or the therapeutic index, is greater than 200,000-fold with this conjugate. These "proof-of-concept" results were presented at the 2002 Ribonuclease Meeting in Bath, England. The NCI has undertaken the manufacturing of RN321 (the conjugate) according to Good Manufacturing Practices, or GMP regulations in preparation for commencing clinical trials for the treatment of patients with non-Hodgkin's lymphoma with RN321. Clinical grade production of RN321 and Investigational New Drug Application, or IND, directed toxicology studies will require further approval from the Drug Development Group of the NIH prior to commencing human clinical trials.

Although ranpirnase is active against a variety of human cancers, its activity is not uniform across different tumor types. However, whether the tumor is more or less sensitive to ranpirnase as a single agent, its anti-tumor activity can be greatly augmented by conjugation to different targeting moieties, or groups. One of these moieties is the epidermal growth factor, or EGF, which is a ligand for the EGF receptor often hyperexpressed on malignant cells. The genetically engineered ranpirnase conjugates with EGF (rRNP-EGF) exerted significant anti-tumor activity in human cell types of the head and neck and pancreatic carcinomas, and human D54MG glioblastoma, a cancerous brain tumor cell. Other constructs target tumor blood vessel formation, which could be potentially used in a broad spectrum of solid tumors. They are in pre-clinical evaluation by our European collaborator.

Novel Amphibian Ribonucleases

All of the proteins characterized to date are RNases. Preclinical testing of the new candidates collectively called amphinases showed them to be similarly active to ranpirnase. Their chemical structure makes them ideal candidates for genetic engineering of designer products.

Research Collaborations

In addition to the above programs, we are pursuing some programs in collaboration with the NIH, NCI and The University of Pennsylvania Medical Center, Metabolic Magnetic Resonance Research and Computing Center.

We have established a number of scientific collaborations with the NIH and NCI. The objective of our collaborations with the NIH and NCI is to develop new therapeutic applications for ONCONASE(R) as well as other drug candidates.

The multiple effects of biological activity of ONCONASE(R) led to research in other areas of cancer biology. Two important areas associated with significant market opportunities are radiation therapy and control of tumor angiogenesis, or new tumor blood vessel formation. Many types of cancers undergo radiation therapy at early stages of the disease; however, success of such treatment is often limited. We believe any agent capable of enhancing tumor radiosensitivity has great market potential. Moreover, since the growth of essentially all types of cancer is dependent on new blood vessel formation, any agent that has anti-angiogenic activity, we believe, is most desirable.

Evaluation Of ONCONASE(R) As A Radiation Enhancer

The p53 gene is a tumor-suppressor gene meaning that if it malfunctions, tumors will develop. Published studies have demonstrated that ONCONASE(R) causes

an increase in both tumor blood flow and in median tumor oxygen partial pressure causing tumor cells to become less resistant to radiation therapy regardless of the presence or absence of the functional p53 tumor-suppressor gene. We believe these findings further expand the profile of ONCONASE(R) in vivo activities and its potential clinical utility and market potential.

The University of Pennsylvania Medical Center, Metabolic Magnetic Resonance Research and Computing Center will further evaluate ONCONASE(R) in combination with radiation and cisplatin, an anti-cancer drug, in human lung adenocarcinoma, a form of lung cancer, in a series of animal models as well as look at the effects of

ONCONASE(R) in the inhibition of sub-lethal damage repair (SLDR) and potentially lethal damage repair (PLDR) in human lung carcinoma cells.

ONCONASE(R) As a Resistance-Overcoming and Apoptosis-Enhancing Agent

The Fas (CD95) cell surface receptor (and its Fas ligand FasL) has been recognized as an important "death" receptor involved in the induction of the "extrinsic" pathway of apoptosis. The apoptotic pathways have been the preferred target for new drug development in cancer, autoimmune, and other therapeutic areas.

The Thoracic Surgery Branch of the NCI confirmed the synergy between ranpirnase and soluble Fas ligand (sFasL) in inducing significant apoptosis in sFasL-resistant Fas+tumor cells. These results provided rationale for using ONCONASE(R) as a potential treatment of FasL-resistant tumors and possibly other disorders such as the autoimmune lympho-proliferative syndrome (ALPS). Further research in this area is ongoing.

Evaluation Of ONCONASE(R) As An Anti-Viral Agent

A collaborative agreement (anti-viral screening, non-SARS) with the National Institute of Allergy and Infectious Diseases, or NIAID, has yielded positive results, which have been confirmed with one of our amphinases. Further evaluation of this potential therapeutic is ongoing.

The ribonucleolytic activity was the basis for testing ONCONASE(R) as a potential anti-viral agent against HIV. The NIH has performed an independent in vitro screen of ONCONASE(R) against the HIV virus type 1. The results showed ONCONASE(R) to inhibit replication of HIV by up to 99.9% after a four-day incubation period at concentrations not toxic to uninfected cells. In vitro findings by the NIH revealed that ONCONASE(R) significantly inhibited production of HIV in several persistently infected human cell lines, preferentially breaking down viral RNA while not affecting normal cellular ribosomal RNA and messenger RNAs, which are essential to cell function.

Moreover, the NIH, Division of AIDS also screened ONCONASE(R) for anti-HIV activity. ONCONASE(R) demonstrated highly significant anti-HIV activity in the monocyte/macrophage, or anti-viral, system. Ranpirnase may inhibit viral replication at several points during the life cycle of HIV, including its early phases. Ranpirnase may inhibit replication of all different HIV-1 subtypes. These properties of ranpirnase are particularly relevant in view of the extremely high and exponentially increasing rate of mutations of HIV that occur during infection, and which are primarily responsible for the development of resistance to several currently available anti-viral drugs. At present, over 50% of clinical isolates of HIV are resistant to both reverse transcriptase, mechanisms which combat viral replication, and protease inhibitors drugs, a

class of anti-viral drugs. An additional 25%, while being sensitive to protease inhibitors, are resistant to RT inhibitor(s) drugs, reverse transcriptase drugs. European collaborators continue to investigate the anti-viral properties of ONCONASE(R). The ribonucleolytic activity of ONCONASE(R) suggested that it might be active against a variety of RNA viruses, including HIV and hepatitis C.

Commercial Collaborations with Pharmaceutical/Drug Delivery Companies

A research and development collaboration with a major US privately held stent and drug delivery company is ongoing. ONCONASE(R) is being evaluated in stents and other delivery platforms to treat cardiovascular disease and cancer via direct site delivery. This collaboration may result in licensing agreement between the companies, however; there is no assurance that such agreement will be reached.

Our research and development collaboration with Wyeth Pharmaceuticals is ongoing to develop a number of designer drugs such as conjugates and fusion proteins for a variety of indications using our proprietary technology. This collaboration may result in a licensing agreement between the companies, however; there is no assurance that such an agreement will be reached.

Raw Materials

The major active ingredient derived from leopard frog eggs is the protein ranpirnase. We have sufficient egg inventory on hand to produce enough ONCONASE(R) to complete the current Phase III clinical trial for malignant mesothelioma and supply ONCONASE(R) for up to two years after commercialization. In addition, we can successfully produce ranpirnase by using recombinant technology; however, it may not be more cost effective.

Manufacturing

We have signed an agreement with Scientific Protein Laboratories, which will perform the intermediary manufacturing process of purifying ranpirnase. We contract with BenVenue Corporation for vial filling and with Cardinal Health for the labeling, storage and shipping of ONCONASE(R) during the Phase III trial period. Other than these arrangements, we do not have specific arrangements for the manufacture of our product. Products manufactured for use in Phase III clinical trials and for commercial sale must be manufactured in compliance with Current Good Manufacturing Practices. Scientific Protein Laboratories, BenVenue Corporation and Cardinal Health all manufacture in accordance with Current Good Manufacturing Practices. For the foreseeable future, we intend to rely on these manufacturers, or substitute manufacturers, if necessary, to manufacture our product. We believe, however, that there are substantial alternative service providers for the services for which we contract. Because we have not yet received drug approval, we utilize the services of these third party manufacturers solely on an as needed basis with prices and terms customary for companies in businesses that are similarly situated. In order to replace an existing manufacturer, we must amend our Investigational New Drug application to notify the FDA of the new manufacturer. We are dependent upon our contract manufacturers to comply with Current Good Manufacturing Practices and to meet our production requirements. It is possible that our contract manufacturers may not comply with Current Good Manufacturing Practices or deliver sufficient quantities of our products on schedule.

Marketing

We do not plan to market our products at this time. We have entered into a

number of Confidential Disclosure Agreements and have been in discussions with several United States and multinational biopharmaceutical companies for the selection of suitable marketing partners for our lead product ONCONASE(R), our proprietary RNA interference technology pipeline, as well as several patented product candidates.

We intend to enter into development and marketing agreements with third parties. We expect that under such arrangements we would grant exclusive marketing rights to our corporate partners in return for assuming further research and development cost, up-front fees, milestone payments and royalties on sales. Under these agreements, our marketing partner may have the responsibility for a significant portion of product development and regulatory approval. In the event that our marketing partner fails to develop a marketable product or fails to market a product successfully, our business may be adversely affected.

Government Regulation

The manufacturing and marketing of pharmaceutical products in the United States requires the approval of the FDA under the Federal Food, Drug and Cosmetic Act. Similar approvals by comparable regulatory agencies are required in most foreign countries. The FDA has established mandatory procedures and safety standards that apply to the clinical testing, manufacturing and marketing of pharmaceutical products in the United States. Obtaining FDA approval for a new therapeutic may take many years and involve substantial expenditures. State, local and other authorities also regulate pharmaceutical manufacturing facilities.

As the initial step in the FDA regulatory approval process, preclinical studies are conducted in laboratory dishes and animal models to assess the drug's efficacy and to identify potential safety problems. Moreover manufacturing processes and controls for the product are required. The manufacturing information along with the results of these studies is submitted to the FDA as a part of the IND, which is filed to obtain approval to begin human clinical testing. The human clinical testing program typically involves up to three phases. Data from human trials as well as other regulatory requirements such as chemistry, manufacturing and controls, pharmacology and toxicology

sections, are submitted to the FDA in an NDA or Biologics License Application, or BLA. Preparing an NDA or BLA involves considerable data collection, verification and analysis. A similar process in accordance with EMEA regulations is required to gain marketing approval in Europe. Moreover, a commercial entity must be established and approved by the EMEA in a member state of the EU at least three months prior to filing the Marketing Authorization Application, or MAA.

We have not received United States or other marketing approval for any of our product candidates and may not receive any approvals. We may encounter difficulties or unanticipated costs in our effort to secure necessary governmental approvals, which could delay or preclude us from marketing our products.

With respect to patented products, delays imposed by the governmental approval process may materially reduce the period during which we may have the exclusive right to exploit them.

Patents and Proprietary Technology

We have protected our business by applying for, and obtaining, patents and trademark registrations. We have also relied on trade secrets and know-how to protect our proprietary technology. We continue to develop our portfolio of patents, trade secrets, and know how. We have obtained, and continue to apply for, patents concerning our RNase-based technology.

In addition, we have filed (and we intend to continue to file) foreign counterparts of certain U.S. patent applications. Generally, we apply for patent protection in the United States, selected European countries, and Japan.

We own the following U.S. patents:

Patent No.	Issue Date	
6,423,515 B1	July 2002	covers methodology for synthesizing gene sequences of ranpirnase and a genetically engineered variant of ra
6,290,951 B1	Sept. 2001	covers alteration of the cell cycle in vivo, particul inducing apoptosis of tumor cells
6,239,257 B1	May 2001	covers a family of variants of ONCONASE(R)
6,175,003 B1	Jan. 2001	covers the genes of ONCONASE(R) and a variant of ONCO
5,728,805	Mar. 1998	covers a family of variants of ONCONASE(R)
5,595,734	Jan. 1997	covers combinations of ONCONASE(R) with certain other pharmaceuticals
5,559,212	Sept. 1996	covers the amino acid sequence of ONCONASE(R)
5,540,925	July 1996	covers combinations of ONCONASE(R) with certain other pharmaceuticals
5,529,775	June 1996	covers combinations of ONCONASE(R) with certain other pharmaceuticals
4,888,172	Dec. 1989	covers a pharmaceutical produced from fertilized frog (Rana pipiens) and the methodology for producing it
6,649,392 B1*	Nov. 2003	covers a family of recombinant variants of ONCONASE(R
6,649,393 B1*	Nov. 2003	covers nucleic acids encoding recombinant variants of and methodology for producing such variants

*We own this patent jointly with the U.S. Government.

We own the following foreign patents in Europe and Japan (European patents are validated in selected European nations):

Patent No.	
EP 0 440 633	covers ONCONASE(R) and process technology for making it
EP 0 500 589 JP 2972334	cover combinations of ONCONASE(R) with certain other pharmaceuticals
EP 0 656 783	covers combinations of ONCONASE(R) with certain other pharmaceuticals
EP 0 837 878	covers a variant of ONCONASE(R)

**Assumes timely payment of all applicable maintenance fees and annuities; excludes term extensions that do or may apply.

These patents cover ONCONASE(R), a variant of ONCONASE(R), process technology for making ONCONASE(R), and combinations of ONCONASE(R) with certain other chemotherapeutics. We also have patent applications pending in the United States, Europe, and Japan.

The scope of protection afforded by patents for biotechnological inventions can be uncertain, and such uncertainty may apply to our patents as well. The patent applications we have filed, or that we may file in the future, may not result in patents. Our patents may not give us competitive advantages, may be wholly or partially invalidated or held unenforceable, or may be held uninfringed by products that compete with our products. Patents owned by others may adversely affect our ability to do business. Furthermore, others may independently develop products that are similar to our products or that duplicate our products, and may design around the claims of our patents. Although we believe that our patents and patent applications are of substantial value to us, we cannot assure you that such patents and patent applications will be of commercial benefit to us, will adequately protect us from competing products or will not be challenged, declared invalid, or uninfringed upon. We also rely on proprietary know-how and on trade secrets to develop and maintain our competitive position. Others may independently develop or obtain access to such know-how or trade secrets. Although our employees and consultants having access to proprietary information are required to sign agreements that require them to keep such information confidential, our employees or consultants may breach these agreements or these agreements may be held to be unenforceable.

Competition

In February 2004, the Food and Drug Administration granted Eli Lilly & Company approval to sell its Alimta(R) medication as an orphan drug to treat patients with pleural mesothelioma. Alimta(R) is a multi-targeted antifolate that is based upon a different mechanism of action than ONCONASE(R). To our knowledge, no other company is developing a product with the same mechanism of action as ONCONASE(R).

There may be several companies, universities, research teams or scientists, which are engaged in research similar, or potentially similar to research performed by us. Some of these entities or persons may have far greater financial resources, larger research staffs and more extensive physical facilities. In addition, these entities or persons may develop products that are more effective than ours and may be more successful than us at producing and

marketing their products.

We are not aware, however, of any product currently being marketed that has the same mechanism of action as our proposed anti-tumor agent, ONCONASE(R). Search of scientific literature reveals no published information that would indicate that others are currently employing this method or producing such an anti-tumor agent. However, we cannot assure you that others may not develop new treatments that are more effective than ONCONASE(R).

Employees

As of September 30, 2004, we have 15 employees, of whom 8 were engaged in research and development activities and 7 were engaged in administration and management. We have 6 employees who hold Ph.D. degrees. All of our employees are covered by confidentiality agreements. We consider relations with our employees to be good. None of our employees are covered by a collective bargaining agreement.

Environmental Matters

Our operations are subject to comprehensive regulation with respect to environmental, safety and similar matters by the United States Environmental Protection Agency and similar state and local agencies. Failure to comply with applicable laws, regulations and permits can result in injunctive actions, damages and civil and criminal penalties. If we expand or change our existing operations or propose any new operations, we may need to obtain additional or amend existing permits or authorizations. We spend time, effort and funds in operating our facilities to ensure compliance with environmental and other regulatory requirements.

Such efforts and expenditures are common throughout the biotechnology industry and generally should have no material adverse effect on our financial condition. The principal environmental regulatory requirements and matters known to us requiring or potentially requiring capital expenditures by us do not appear likely, individually or in the aggregate, to have a material adverse effect on our financial condition. We believe that we are in compliance with all current laws and regulations.

Item 2. PROPERTIES.

We lease a total of approximately 17,000 square feet in an industrial office building located in Bloomfield, New Jersey on a month-to-month basis. The monthly rental obligation is $11,333. We believe that the facility is sufficient for our needs in the foreseeable future.

Item 3. LEGAL PROCEEDINGS.

We are presently not involved in any legal proceedings.

Item 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS.

None.

Part II

Item 5. MARKET FOR COMMON EQUITY AND RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES.

Our common stock is listed on the The Nasdaq SmallCap Market, or Nasdaq, and has traded under the symbol "ACEL" since September 9, 2004. As of October 8, 2004, there were approximately 1,112 stockholders of record of our common stock.

The following table sets forth the range of high and low sale prices of our common stock for the two fiscal years ended July 31, 2004 and 2003. The prices were obtained from OTCBB and are believed to be representative of inter-dealer quotations, without retail mark-up, mark-down or commission, and may not necessarily represent actual transactions.

	High	Low
Year Ended July 31, 2004:		
First Quarter	$4.51	$1.25
Second Quarter	5.14	2.65

	High	Low
Third Quarter	9.97	3.70
Fourth Quarter	10.07	5.50
Year Ended July 31, 2003:		
First Quarter	0.36	$ 0.18
Second Quarter	1.01	0.19
Third Quarter	0.85	0.39
Fourth Quarter	1.45	0.64

We have not paid dividends on our common stock since inception and we do not plan to pay dividends in the foreseeable future. Any earnings we may realize will be retained to finance our growth.

The following table provides additional information on the Company's equity based compensation plans as of July 31, 2004:

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted-average exercise price of outstanding options, warrants and rights (b)	Numb remai futu equity (exc refle
Equity compensation plans approved by security holders	2,957,445	$ 2.95	
Equity compensation plans not approved by security holders	55,556 (1)	$ 1.50	

(1) In August 2001, we converted $50,000 of our accounts payable into 55,556 shares of common stock. In addition, we issued 55,556 five-year warrants to purchase 55,556 shares of common stock at an exercise price of $1.50 per share.

Recent Sales of Unregistered Securities

The following is a summary of transactions involving our securities from May 1, 2004 to July 31, 2004. Each of the following was exempt from registrations under Section 4(2) of the Securities Act of 1933, as amended, based upon the fact that each issuance was to an accredited investor. The net proceeds from these transactions were used for general corporate purposes, including the funding of research and development.

In May 2004, we issued 1,210,654 shares of Common Stock to an existing institutional investor, resulting in gross proceeds of $10,000,000 to us. In addition, the institutional investor was granted five-year warrants to purchase 1,210,654 shares of Common Stock at an exercise price of $12.39 per share. We paid a 5% finder's fee and granted a five-year warrant to purchase 60,533 shares of Common Stock at an exercise price of $12.39 per share to a third party in connection with the private placement.

In May and June 2004, we issued, an aggregate of 785,000 shares of restricted common stock upon the exercise of warrants by unrelated parties, at per share exercise prices ranging from $0.75 to $1.50. We realized aggregate gross proceeds of $1,051,250 from these exercises.

In May 2004, we issued 25,000 shares of restricted common stock as payment for services rendered in the amount of $198,500.

In June 2004, we issued 2,099 restricted shares of common stock as payment of accounts payable in the amount of $9,447.

From June 2004 through July 15, 2004, we issued an aggregate of 1,574,424 shares of restricted common stock and 1,815,466 shares of common stock underlying five-year warrants with exercise prices ranging from $1.00 to $1.10 per share upon the conversion of notes payable by unrelated parties in an aggregate amount of $413,275.

Issuer Purchases of Equity Securities

We did not repurchase any shares of our common stock during the fourth quarter of fiscal 2004.

Item 6. SELECTED FINANCIAL DATA.

Set forth below is the selected financial data for our company for the five fiscal years ended July 31, 2004.

	Year Ended July 31,			
	2004	2003	2002	2001

Investment Income	$ 42,113	$ 9,877	$ 4,838	$ 13,121	$
Other Income	--	30,000	--	--	
Net Loss (1)	(5,070,307)	(2,411,532)	(2,591,162)	(2,294,936)	(1,
Net Loss Per Basic and Diluted Share	(.17)	(.10)	(.12)	(.12)	
Dividends	None	None	None	None	
Total Assets	10,421,063	495,322	228,871	201,609	
Long-term Debt	--	242,516	315,929	23,663	
Total Equity (Deficiency)	8,881,647	(2,491,681)	$(1,885,437)	(740,378)	(

(1) Included in the net loss of $5,070,307, $2,411,532 and $2,591,162 for fiscal years ended July 31, 2004, 2003 and 2002, respectively, are tax benefits of $221,847, $231,357 and $353,732, respectively, related to the sale of certain state tax operating loss carryforwards.

Item 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.

Overview

Since our inception, we have devoted the vast majority of our resources to the research and development of ONCONASE(R) and related drug candidates. We have focused our resources towards the completion of the clinical program for unresectable, or inoperable, malignant mesothelioma.

Since ONCONASE(R) has Fast Track Designation for the treatment of malignant mesothelioma patients, we continue to have meetings and discussions with the FDA to establish mutually agreed upon parameters for the New Drug Application, or NDA to obtain marketing approval for ONCONASE(R), assuming the Phase III clinical trial for the treatment of malignant mesothelioma yields favorable results.

We received an Orphan Medicinal Product Designation for ONCONASE(R) from the European Agency for the Evaluation of Medicinal Products, or the EMEA. We continue to fulfill the EMEA requirements regarding the Marketing Authorization Application, or MAA registration requirements for ONCONASE(R) for the treatment of malignant mesothelioma.

Almost all of our research and development expenses since our inception of $44,954,912 has gone toward the development of ONCONASE(R) and related drug candidates. For the fiscal years 2004, 2003 and 2002 our research and development expenses were $3,353,000, $1,700,000 and $2,033,000, respectively, almost all of which was used for the development of ONCONASE(R) and related drug candidates. ONCONASE(R) is currently in an international, centrally randomized Phase III trial. The first part of the trial has been completed and the second confirmatory part of the trial is ongoing for which patient enrollment is expected to be completed in the first quarter of 2005. The primary endpoint of

the trial is survival, and as such, a sufficient number of deaths must occur in order to perform the required statistical analyses to determine the efficacy of ONCONASE(R) in patients with unresectable (inoperable) malignant mesothelioma. If the results of the clinical trials are positive, we expect to file for marketing registrations (NDA and MAA) for ONCONASE(R) within six months of completion of the statistical analyses. However, at this time, we cannot predict with certainty when a sufficient number of deaths will occur to achieve statistical significance. Hence, the timing of when we will be able to file for marketing registrations in the US and EU is data driven. Therefore, we cannot predict with certainty what our total cost associated with obtaining marketing approvals will be, or when and if such approvals will be granted, or when actual sales will occur.

We fund the research and development of our products from cash receipts resulting from the sale of our equity securities and convertible debentures in registered offerings and private placements. Additionally, we have raised capital through debt financings, the sale of our tax benefits and research products, interest income and financing received from our Chief Executive Officer. Presently, our cash balance is sufficient to fund our expanded operations at least through October 31, 2005 based on our expected level of expenditures in relation to activities in preparing ONCONASE(R) for marketing registrations and other ongoing operations of the Company. However, we continue to seek additional capital financing through the sale of equity in private placements, sale of our tax benefits and exercise of stock options and warrants but cannot be sure that we will be able to raise capital on favorable terms or at all.

Results of Operations

Fiscal Years Ended July 31, 2004, 2003 and 2002

Revenues

We are a development stage company as defined in the Financial Accounting Standards Board's Statement of Financial Accounting Standards No. 7. We are devoting substantially all our present efforts to establishing a new business and developing new drug products. Our planned principal operations of marketing and/or licensing of new drugs have not commenced and, accordingly, we have not derived any significant revenue from these operations. We focus most of our productive and financial resources on the development of ONCONASE(R). We did not have

any sales in fiscal 2004, 2003 and 2002. Investment income for fiscal 2004 was $42,000 compared to $10,000 for fiscal 2003, an increase of $32,000. Investment income for fiscal 2003 was $10,000 compared to $5,000 for fiscal 2002, an increase of $5,000. These increases were due to higher balances of cash and cash equivalents. Other income for fiscal 2003 was related to investigational research we performed for a pharmaceutical company.

Research and Development

Research and development expense for fiscal 2004 was $3,353,000 compared to $1,700,000 for fiscal 2003, an increase of $1,653,000, or 97%. This increase was primarily due to increases in data management, consulting fees and clinical expenses related to our pivotal Phase III clinical trial for malignant mesothelioma of approximately $1,302,000, sponsored research and development expenses of approximately $236,000, regulatory consulting costs of approximately $142,000, non cash expense related to stock options issued for consulting

services of approximately $94,000, offset by a decrease in personnel and insurance expenses of approximately $121,000.

Research and development expense for fiscal 2003 was $1,700,000 compared to $2,033,000 for fiscal 2002, a decrease of $333,000, or 16.4%. This decrease was primarily due to decreases in regulatory and clinical costs, personnel costs, and a reduction of non-cash expenses relating to stock options issued for consulting services of approximately $236,000, $114,000 and $23,000, respectively. These decreases were partially offset by increases in costs relating to patent and trademark applications for ONCONASE(R) of approximately $40,000.

General and Administrative

General and administrative expense for fiscal 2004 was $1,578,000 compared to $624,000 for fiscal 2003, an increase of $954,000, or 153%. The increase was due primarily to an increase in non-cash expense related to stock and stock options issued for consulting services associated with business development activities of approximately $402,000, increases in legal, public relations, personnel, insurance, and accounting expenses of approximately $230,000, $109,000, $106,000, $77,000 and $30,000, respectively.

General and administrative expense for fiscal 2003 was $624,000 compared to $798,000 for fiscal 2002, a decrease of $174,000, or 21.8%. This decrease was primarily due to decreases in costs related to public relations activities, insurance expenses, reduction in non-cash expense relating to stock options issued for consulting services, legal, personnel costs and other miscellaneous office expenses of approximately $71,000, $54,000, $34,000, $10,000 and $5,000, respectively.

Interest

Interest expense for fiscal 2004 was $403,000 compared to $358,000 in fiscal 2003, an increase of $45,000 or 12.6%. The increase was primarily due to the interest expense on the beneficial conversion feature of the notes payable and its related warrants issued to unrelated parties. The interest expense was based on the value of the warrants using the Black-Scholes options-pricing model, amortized on a straight-line basis over the term of the notes.

Interest expense for fiscal 2003 was $358,000 compared to $119,000 in fiscal 2002, an increase of $239,000. The increase was primarily due to the interest expense on the beneficial conversion feature of the notes payable issued to unrelated parties, the related warrants and the increase in total borrowing levels. The interest expense was based on the value of the warrants using the Black-Scholes options-pricing model, amortized on a straight-line basis over the term of the notes.

Income Taxes

New Jersey has enacted legislation permitting certain corporations located in New Jersey to sell state tax loss carryforwards and state research and development credits, or tax benefits. For the state fiscal year 2004 (July 1, 2003 to June 30, 2004), we had approximately $1,378,000 total available tax benefits that were saleable; of which New Jersey permitted us to sell approximately $261,000. We received approximately $222,000 from the sale of the $261,000 of tax benefits, which we recognized as tax benefits for the fiscal year ended July 31, 2004.

For the state fiscal year 2003 (July 1, 2002 to June 30, 2003), we had approximately $1,373,000 in total available tax benefits that were saleable; of which New Jersey permitted us to sell approximately $273,000. We received approximately $231,000 from the sale of the $273,000 of tax benefits, which we recognized as tax benefits for the fiscal year ended July 31, 2003.

For the state fiscal year 2002 (July 1, 2001 to June 30, 2002), we had approximately $1,535,000 total available tax benefits that were saleable; of which New Jersey permitted us to sell approximately $426,000. We received approximately $354,000 from the sale of the $426,000 of tax benefits, which we recognized as tax benefits for fiscal 2002.

If still available under New Jersey law, we will attempt to sell the remaining $1,117,000 of our tax benefits, between July 1, 2004 and June 30, 2005. This amount, which is a carryover of our remaining tax benefits from state fiscal year 2004, may increase if we incur additional tax benefits during state fiscal year 2005. We can not estimate, however, what percentage of our saleable tax benefits New Jersey will permit us to sell, how much money we will receive in connection with the sale, if we will be able to find a buyer for our tax benefits or if such funds will be available in a timely manner.

Net Loss

We have incurred net losses during each year since our inception. The net loss for fiscal 2004 was $5,070,000 as compared to $2,411,000 in fiscal 2003 and $2,591,000 in fiscal 2002. The cumulative loss from the date of inception, August 24, 1981, to July 31, 2004 amounted to $69,045,000. Such losses are attributable to the fact that we are still in the development stage and, accordingly, have not derived sufficient revenues from operations to offset the development stage expenses.

Liquidity and Capital Resources

We have reported net losses of approximately $5,070,000, $2,411,000, and $2,591,000 for the fiscal years ended July 31, 2004, 2003 and 2002, respectively. The loss from date of inception, August 24, 1981, to July 31, 2004 amounts to $69,045,000.

We have financed our operations since inception through the sale of our equity securities and convertible debentures in registered offerings and private placements. Additionally, we have raised capital through debt financings, the sale of our tax benefits and research products, and interest income and financing received from our Chief Executive Officer. During the fiscal year 2004, we had a net increase in cash and cash equivalents of $9,818,000, which resulted primarily from net cash provided by financing activities of $14,886,000, which resulted from $10,736,000 in net proceeds from private placements of common stock and warrants with several institutional investors, $4,158,000 in net proceeds from warrants and stock options exercises and a reduction in short term debt of $9,000, offset by net cash used in operating activities of $5,015,000, principally for research and development activities, and net cash used in investing activities of $54,000. Total cash resources as of July 31, 2004 were $10,148,000 compared to $330,000 at July 31, 2003.

Our current liabilities as of July 31, 2004 were $1,539,000 compared to $2,744,000 at July 31, 2003, a decrease of $1,205,000. The decrease was primarily due to the payment of accrued payroll of $644,000 and payroll taxes of $241,000, maturity of short-term notes payable of approximately $264,000 and decreased accounts payable and other accrued expenses of approximately $56,000.

The following transactions occurred after July 31, 2004:

- In September 2004, we issued 320,157 shares of restricted common stock and an aggregate of 420,157 shares of common stock underlying five year warrants with an exercise price of $1.00 per share upon the conversion of notes payable in the amount of $112,055.

- In September 2004, we issued an aggregate of 292,272 shares of restricted common stock upon the exercise of warrants and stock options by a board member and unrelated parties at exercise prices ranging from $0.29 to $1.50 per share. We realized aggregate gross proceeds of $224,054 from these exercises.

Our continued operations will depend on our ability to raise additional funds through various potential sources such as equity and debt financing, collaborative agreements, strategic alliances, sale of tax benefits, revenues from the commercial sale of ONCONASE(R), licensing of our proprietary RNase technology and our ability to realize revenues from our technology and our drug candidates via out-licensing agreements with other companies. Such additional funds may not become available as we need them or be available on acceptable terms. Through October 14, 2004, a significant portion of our financing has been through the sale of our equity securities and convertible debentures in registered offerings and private placements and exercise of stock options and warrants. Additionally, we have raised capital through debt financings, the sale of our tax benefits and research products, interest income and financing received from our Chief Executive Officer. Until and unless our operations generate significant revenues, we expect to continue to fund operations from the sources of capital previously described. There can be no assurance that we will be able to raise the capital we need on terms which are acceptable, if at all. Presently, our cash balance is sufficient to fund our expanded operations at least through October 31, 2005, based on our expected level of expenditures in relation to activities in preparing ONCONASE(R) for marketing registrations and other ongoing operations of the Company. However, we continue to seek additional capital financing through the sale of equity in private placements, sale of our tax benefits and exercise of stock options and warrants but cannot be sure that we will be able to raise capital on favorable terms or at all.

We will continue to incur costs in conjunction with our U.S. and foreign registrations for marketing approval of ONCONASE(R). We are currently in discussions with potential strategic alliance partners to further the development and marketing of ONCONASE(R) and other related products in our pipeline. However, we cannot be sure that any such alliances will materialize.

The market price of our Common Stock is volatile, and the price of the stock could be dramatically affected one way or another depending on numerous factors. The market price of our Common Stock could also be materially affected by the marketing approval or lack of approval of ONCONASE(R).

Off-balance Sheet Arrangements

As part of our ongoing business, we do not participate in transactions that generate relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities or SPE, which would have been established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. As of July 31, 2004, we are not involved in any material unconsolidated SPE transactions.

Critical Accounting Policies

In December 2001, the SEC requested that all registrants discuss their

most "critical accounting policies" in management's discussion and analysis of financial condition and results of operations. The SEC indicated that a "critical accounting policy" is one which is both important to the portrayal of the company's financial condition and results and requires management's most difficult, subjective or complex judgments, often as a result of the need to make estimates about the effect of matters that are inherently uncertain. The accounting policies set forth below have been considered critical because changes to certain judgments, estimates and assumptions could significantly affect our financial statements.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues, expenses and related disclosures during the reporting period. Since some of those estimates are subjective and complex, actual results could differ from those estimates.

Research and Development

Research and development costs are expensed as incurred.

Accounting For Stock-Based Compensation

Statements of Financial Accounting Standards No. 123, Accounting for Stock-Based Compensation ("SFAS 123"), provides for the use of a fair value based method of accounting for employee stock compensation. However, SFAS 123 also allows an entity to continue to measure compensation cost for stock options granted to employees and directors using the intrinsic value method of accounting prescribed by Accounting Principles Board Opinion No. 25, Accounting for Stock Issued to Employees ("APB 25"), which only requires charges to compensation expense for the excess, if any, of the fair value of the underlying stock at the date a stock option is granted (or at an appropriate subsequent measurement date) over the amount the employee must pay to acquire the stock, if such amounts differ materially from the historical amounts. We have elected to continue to account for employee stock options using the intrinsic value method under Opinion 25.

Pursuant to SFAS 123, shares, warrants or options issued in connection with debt financing agreements or to non-employees for services are accounted for based on their fair market value determined using the Black-Scholes option pricing model.

Accounting For Warrants Issued With Convertible Debt

We account for the intrinsic value of beneficial conversion rights arising from the issuance of convertible debt instruments with nondetachable conversion rights that are in-the-money at the commitment date pursuant to the consensuses for EITF Issue No. 98-5 and EITF Issue No. 00-27. Such value is allocated to additional paid-in capital and the resulting debt discount is charged to interest expense over the terms of the notes payable. Such value is determined after first allocating an appropriate portion of the proceeds received to warrants or any other detachable instruments included in the exchange.

Income Taxes

We account for income taxes under the provisions of Statement of Financial

Accounting Standards No. 109, "Accounting for Income Taxes" (SFAS No. 109). Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement carrying amounts and tax bases of assets and liabilities using enacted tax rates in effect for all years in which the temporary differences are expected to reverse. A valuation allowance is provided when it is more likely than not that some portion or all of the deferred tax assets will not be realized.

Contractual Obligations and Commercial Commitments

Our major outstanding contractual obligations relate to our equipment operating lease. Below is a table that presents our contractual obligations and commercial commitments as of July 31, 2004:

	Payments Due by Fiscal Year		
	Total	2005	2006 and Thereafter
Research and development	$72,398	$72,398	$ -0-
Operating lease	13,100	13,100	-0-
Total contractual cash obligations	$85,498	$85,498	$ -0-

RISK FACTORS

An investment in our common stock is speculative and involves a high degree of risk. You should carefully consider the risks and uncertainties described below and the other information in this Form 10-K and our other SEC filings before deciding whether to purchase shares of our common stock. If any of the following risks actually occur, our business and operating results could be harmed. This could cause the trading price of our common stock to decline, and you may lose all or part of your investment.

We have incurred losses since inception and anticipate that we will incur continued losses for the foreseeable future. We do not have a current source of product revenue and may never be profitable.

We are a development stage company and since our inception our source of working capital has been public and private sales of our stock. We incurred a net loss of approximately $5,070,000 for the fiscal year ended July 31, 2004. We have continued to incur losses since July 2004. We may never achieve revenue sufficient for us to attain profitability.

We incurred net losses of approximately $5,070,000, $2,411,000 and $2,591,000 for the fiscal years ended July 31, 2004, 2003 and 2002, respectively.

Our profitability will depend on our ability to develop, obtain regulatory approvals for, and effectively market ONCONASE(R) as well as entering into strategic alliances for the development of new drug candidates from the out-licensing of our proprietary RNase technology. The commercialization of our pharmaceutical products involves a number of significant challenges. In particular our ability to commercialize ONCONASE(R) depends on the success of our clinical development programs, our efforts to obtain regulatory approval and our sales and marketing efforts or those of our marketing partners, if any,

directed at physicians, patients and third-party payors. A number of factors could affect these efforts including:

- Our ability to demonstrate clinically that our products have utility and are safe;
- Delays or refusals by regulatory authorities in granting marketing approvals;
- Our limited financial resources relative to our competitors;
- Our ability to obtain an appropriate marketing partner;
- The availability and level of reimbursement for our products by third party payors;
- Incidents of adverse reactions to our products;
- Side effects or misuse of our products and unfavorable publicity that could result; and
- The occurrence of manufacturing or distribution disruptions.

We will seek to generate revenue through licensing, marketing and development arrangements prior to receiving revenue from the sale of our products. To date we have not consummated any licensing or marketing arrangements and we may not be able to successfully consummate any such arrangements. We have entered into several development arrangements, which have resulted in limited revenues for us. However, we cannot ensure that these arrangements or future arrangements, if any, will result in significant amounts of revenue for us. We, therefore, are unable to predict the extent of any future losses or the time required to achieve profitability, if at all.

We need additional financing to continue operations, which may not be available on acceptable terms, if it is available at all.

We need additional financing in order to continue operations, including completion of our current clinical trials and filing marketing registrations for ONCONASE(R) in the United States with the FDA and in Europe with the

EMEA. If the results from our current clinical trial do not demonstrate the efficacy and safety of ONCONASE(R) for malignant mesothelioma, our ability to raise additional capital will be adversely affected. Even if regulatory applications for marketing approvals are filed, we will need additional financing to continue operations. In connection with the recent private placement from which we realized $10.0 million in gross proceeds from an institutional investor, we plan to expand our operations in preparing ONCONASE(R) for marketing registrations in the US and outside the US as well as fund our ongoing operations. Presently, our cash balance is sufficient to fund our expanded operations at least through October 31, 2005, based on our expected level of expenditures. However, taking into consideration all of the uncertainties related to drug development and our industry, we continue to seek additional capital financing through the sale of equity in private placements, sale of our tax benefits and exercise of stock options and warrants but cannot be sure that we will be able to raise capital on favorable terms or at all.

We may be unable to sell certain state tax benefits in the future and if we are unable to do so, it would eliminate a source of financing that we have relied on

in the past.

At July 31, 2004, we had federal net operating loss carryforwards of approximately $47,326,000 that expire from 2005 to 2024. We also had research and experimentation tax credit carryforwards of approximately $1,426,000 that expire from 2005 to 2024. New Jersey has enacted legislation permitting certain corporations located in New Jersey to sell state tax loss carryforwards and state research and development credits or tax benefits. The aggregate amount of tax benefits that New Jersey allows corporations to sell each state fiscal year (July 1st through June 30th) is determined annually and if New Jersey reduces such aggregate amount in any fiscal year we may be unable to sell some or all of our available tax benefits as we have in the past. In addition, there is a limited market for these types of sales and we may not be able to find someone to purchase our tax benefits for a reasonable price. Our historical results of operations have been improved by our sale of tax benefits and if we continue to generate a limited amount of revenue and are unable in the future to sell our tax benefits, our results of operations will be negatively impacted.

For the state fiscal year 2004 (July 1, 2003 to June 30, 2004), we had approximately $1,378,000 total available tax benefits that were saleable; of which New Jersey permitted us to sell approximately $261,000. We received approximately $222,000 from the sale of the $261,000 of tax benefits, which we recognized as tax benefits for the fiscal year ended July 31, 2004. For the state fiscal year 2003 (July 1, 2002 to June 30, 2003), we had approximately $1,373,000 in total available tax benefits that were saleable; of which New Jersey permitted us to sell approximately $273,000. We received approximately $231,000 from the sale of the $273,000 of tax benefits, which we recognized as tax benefits for the fiscal year ended July 31, 2003.

If still available under New Jersey law, we will attempt to sell the remaining $1,117,000 of our tax benefits, between July 1, 2004 and June 30, 2005. This amount, which is a carryover of our remaining tax benefits from state fiscal year 2004, may increase if we incur additional tax benefits during state fiscal year 2005. We can not estimate, however, what percentage of our sellable tax benefits New Jersey will permit us to sell, how much money we will receive in connection with the sale, if we will be able to find a buyer for our tax benefits or if such funds will be available in a timely manner.

We cannot predict how long it will take us nor how much it will cost us to complete our Phase III trial because it is a survival study and we are still in patient enrollment in part two of this Phase III trial.

We currently have ongoing a two-part Phase III trial of ONCONASE(R) as a treatment for malignant mesothelioma. The first part of the clinical trial has been completed and the second, confirmatory part is still ongoing for which patient enrollment is expected to be completed in the first quarter of 2005. The primary endpoint of the Phase III clinical trial is survival, which tracks the length of time patients enrolled in the study live. According to the protocol, a sufficient number of patient deaths must occur in order to perform the required statistical analyses to determine the efficacy of ONCONASE(R) in patients with unresectable (inoperable) malignant mesothelioma. Since it is impossible to predict with certainty when these terminal events in the Phase III trial will occur, we do not have the capability of reasonably determining when a sufficient number of deaths will occur, nor when we will be able to file for marketing registrations with the FDA and EMEA.

In addition, clinical trials are very costly and time consuming. The length of time required to complete a clinical trial depends on several factors

including the size of the patient population, the ability of patients to get to the site of the clinical study, and the criteria for determining which patients are eligible to join the study. Delays in patient enrollment, could delay achieving a sufficient number of deaths required for statistical analyses, which therefore may delay the marketing registrations. Although we believe we could modify some of our expenditures to reduce our cash outlays in relation to our clinical trials and other NDA related expenditures, we cannot quantify which or the amount such expenditures might be modified. Hence, a delay in the commercial sale of ONCONASE(R) would increase the time frame of our cash expenditure outflows and may require us to seek additional financing. Such capital financing may not be available on favorable terms or at all.

The FDA and comparable regulatory agencies in foreign countries impose substantial pre-market approval requirements on the introduction of pharmaceutical products. These requirements involve lengthy and detailed pre-clinical and clinical testing and other costly and time consuming procedures. Satisfaction of these requirements typically takes several years depending on the type, complexity and novelty of the product. We cannot apply for FDA or EMEA approval to market ONCONASE(R) until the clinical trials and all other registration requirements have been met.

If we fail to obtain the necessary regulatory approvals, we will not be allowed to commercialize our drugs and will not generate product revenue.

The FDA and comparable regulatory agencies in foreign countries impose substantial pre-market approval requirements on the introduction of pharmaceutical products. These requirements involve lengthy and detailed pre-clinical and clinical testing and other costly and time consuming procedures. Satisfaction of these requirements typically takes several years depending on the level of complexity and novelty of the product. Drugs in late stages of clinical development may fail to show the desired safety and efficacy results despite having progressed through initial clinical testing. While limited trials with our product have produced certain favorable results, we cannot be certain that we will successfully complete Phase I, Phase II or Phase III testing of any compound within any specific time period, if at all. Furthermore, the FDA or the company may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. In addition, we cannot apply for FDA or EMEA approval to market ONCONASE(R) until pre-clinical and clinical trials have been completed. Several factors could prevent the successful completion or cause significant delays of these trials including an inability to enroll the required number of patients or failure to demonstrate the product is safe and effective in humans. Also if safety concerns develop, the FDA and EMEA could stop our trials before completion.

In December 2002, we received Fast Track Designation from the Food and Drug Administration, or the FDA for ONCONASE(R) for the treatment of malignant mesothelioma. In February 2001, we received an Orphan Medicinal Product Designation for ONCONASE(R) from the European Agency for the Evaluation of Medicinal Products, or the EMEA.

All statutes and regulations governing the conduct of clinical trials are subject to change by various regulatory agencies, including the FDA, in the future, which could affect the cost and duration of our clinical trials. Any unanticipated costs or delays in our clinical studies would delay our ability to generate product revenues and to raise additional capital and could cause us to be unable to fund the completion of the studies.

We may not market or sell any product for which we have not obtained regulatory approval. We cannot assure that the FDA or other regulatory agencies will ever approve the use of our products that are under development. Even if we receive regulatory approval, such approval may involve limitations on the

indicated uses for which we may market our products. Further, even after approval, discovery of previously unknown problems could result in additional restrictions, including withdrawal of our products from the market.

If we fail to obtain the necessary regulatory approvals, we cannot market or sell our products in the United States, or in other countries and our long-term viability would be threatened. If we fail to achieve regulatory approval or foreign marketing authorizations for ONCONASE(R) we will not have a saleable product or product revenues for quite some time, if at all, and may not be able to continue operations.

We are and will be dependent upon third parties for manufacturing our products. If these third parties do not devote sufficient time and resources to our products our revenues and profits may be adversely affected.

We do not have the required manufacturing facilities to manufacture our products. We presently rely on third parties to perform certain of the manufacturing processes for the production of ONCONASE(R) for use in clinical trials. Currently, we contract with Scientific Protein Labs for the manufacturing of ranpirnase (protein drug substance) from the oocytes, or the unfertilized eggs, of the Rana pipiens frog, which is found in the Northwest United States and is commonly called the leopard frog. We contract with Ben Venue Corporation for the manufacturing of ONCONASE(R) and with Cardinal Health for the labeling, storage and shipping of ONCONASE(R) for clinical trial use. We utilize the services of these third party manufacturers solely on an as needed basis with terms and prices customary for our industry.

Our use of manufacturers for ranpirnase and ONCONASE(R) have been approved by the FDA. We have identified substantial alternative service providers for the manufacturing services for which we contract. In order to replace an existing service provider we must amend our IND to notify the FDA of the new manufacturer. Although the FDA generally will not suspend or delay a clinical trial as a result of replacing an existing manufacturer, the FDA has the authority to suspend or delay a clinical trial if, among other grounds, human subjects are or would be exposed to an unreasonable and significant risk of illness or injury as a result of the replacement manufacturer.

We intend to rely on third parties to manufacture our products if they are approved for sale by the appropriate regulatory agencies and are commercialized. Third party manufacturers may not be able to meet our needs with respect to the timing, quantity or quality of our products or to supply products on acceptable terms.

Because we do not have marketing, sales or distribution capabilities, we expect to contract with third parties for these functions and we will therefore be dependent upon such third parties to market, sell and distribute our products in order for us to generate revenues.

We currently have no sales, marketing or distribution capabilities. In order to commercialize any product candidates for which we receive FDA approval, we expect to rely on established third party strategic partners to perform these functions. For example, if we are successful in our Phase III clinical trials with ONCONASE(R), and are granted marketing approval for the commercialization of ONCONASE(R), we will be unable to introduce the product to market without establishing a marketing collaboration with a pharmaceutical company with those resources. If we establish relationships with one or more biopharmaceutical or other marketing companies with existing distribution systems and direct sales forces to market any or all of our product candidates, we cannot assure you that

we will be able to enter into or maintain agreements with these companies on acceptable terms, if at all. Further, it is likely that we will have limited or no control over the manner in which product candidates are marketed or the resources devoted to such markets.

In addition, we expect to begin to incur significant expenses in determining our commercialization strategy with respect to one or more of our product candidates. The determination of our commercialization strategy with respect to a product candidate will depend on a number of factors, including:

- the extent to which we are successful in securing collaborative partners to offset some or all of the funding obligations with respect to product candidates;
- the extent to which our agreement with our collaborators permits us to exercise marketing or promotion rights with respect to the product candidate;
- how our product candidates compare to competitive products with respect to labeling, pricing, therapeutic effect, and method of delivery; and
- whether we are able to establish agreements with third party collaborators, including large biopharmaceutical or other marketing companies, with respect to any of our product candidates on terms that are acceptable to us.

A number of these factors are outside of our control and will be difficult to determine.

Our product candidates may not be accepted by the market.

Even if approved by the FDA and other regulatory authorities, our product candidates may not achieve market acceptance, which means we would not receive significant revenues from these products. Approval by the FDA does not necessarily mean that the medical community will be convinced of the relative safety, efficacy and cost-effectiveness of our products as compared to other products. In addition, third party reimbursers such as insurance companies and HMOs may be reluctant to reimburse expenses relating to our products.

We depend upon Kuslima Shogen and our other key personnel and may not be able to retain these employees or recruit qualified replacement or additional personnel, which would have a material adverse affect on our business.

We are highly dependent upon our founder, Chairman and Chief Executive Officer, Kuslima Shogen. Kuslima Shogen's talents, efforts, personality, vision and leadership have been, and continue to be, critical to our success. The diminution or loss of the services of Kuslima Shogen, and any negative market or industry perception arising from that diminution or loss, would have a material adverse effect on our business. While our other employees have substantial experience and have made significant contributions to our business, Kuslima Shogen is our senior executive and also our primary supporter because she represents the Company's primary means of accessing the capital markets.

Because of the specialized scientific nature of our business, our continued success also is dependent upon our ability to attract and retain qualified management and scientific personnel. There is intense competition for qualified personnel in the pharmaceutical field. As our company grows our

inability to attract qualified management and scientific personnel could materially adversely affect our research and development programs, the commercialization of our products and the potential revenue from product sales.

We do not have employment contracts with Kuslima Shogen or any of our other management and scientific personnel.

Our proprietary technology and patents may offer only limited protection against infringement and the development by our competitors of competitive products.

We own two patents jointly with the United States government. These patents expire in 2016. We also own ten United States patents with expiration dates ranging from 2006 to 2019, four European patents with expiration dates ranging from 2009 to 2016 and one Japanese patent that expires in 2010. We also own patent applications that are pending in the United States, Europe and Japan. The scope of protection afforded by patents for biotechnological inventions is uncertain, and such uncertainty applies to our patents as well. Therefore, our patents may not give us competitive advantages or afford us adequate protection from competing products. Furthermore, others may independently develop products that are similar to our products, and may design around the claims of our patents. Patent litigation and intellectual property litigation are expensive and our resources are limited. If we were to become involved in litigation, we might not have the funds or other resources necessary to conduct the litigation effectively. This might prevent us from protecting our patents, from defending against claims of infringement, or both. To date, we have not received any threats of litigation, legal actions or negotiations regarding patent issues.

Developments by competitors may render our products obsolete or non-competitive.

In February 2004, the Food and Drug Administration granted Eli Lilly & Company approval to sell its Alimta(R) medication as an orphan drug to treat patients with pleural mesothelioma. Alimta is a multi-targeted antifolate that is based upon a different mechanism of action than ONCONASE(R). To our knowledge, no other company is developing a product with the same mechanism of action as ONCONASE(R). However, there may be other companies, universities, research teams or scientists who are developing products to treat the same medical conditions our products are intended to treat. Eli Lilly is, and some of these other companies, universities, research teams or scientists may be more experienced and have greater clinical, marketing and regulatory capabilities and managerial and financial resources than we do. This may enable them to develop products to treat the same medical

conditions our products are intended to treat before we are able to complete the development of our competing product.

Our business is very competitive and involves rapid changes in the technologies involved in developing new drugs. If others experience rapid technological development, our products may become obsolete before we are able to recover expenses incurred in developing our products. We will probably face new competitors as new technologies develop. Our success depends on our ability to remain competitive in the development of new drugs or we may not be able to compete successfully.

We may be sued for product liability.

Our business exposes us to potential product liability that may have a negative effect on our financial performance and our business generally. The administration of drugs to humans, whether in clinical trials or commercially,

exposes us to potential product and professional liability risks which are inherent in the testing, production, marketing and sale of new drugs for humans. Product liability claims can be expensive to defend and may result in large judgments or settlements against us, which could have a negative effect on our financial performance and materially adversely affect our business. We maintain product liability insurance to protect our products and product candidates in amounts customary for companies in businesses that are similarly situated, but our insurance coverage may not be sufficient to cover claims. Furthermore, liability insurance coverage is becoming increasingly expensive and we cannot be certain that we will always be able to maintain or increase our insurance coverage at an affordable price or in sufficient amounts to protect against potential losses. A product liability claim, product recall or other claim, as well as any claim for uninsured liabilities or claim in excess of insured liabilities, may significantly harm our business and results of operations. Even if a product liability claim is not successful, adverse publicity and time and expense of defending such a claim may significantly interfere with our business.

If we are unable to obtain favorable reimbursement for our product candidates, their commercial success may be severely hindered.

Our ability to sell our future products may depend in large part on the extent to which reimbursement for the costs of our products is available from government entities, private health insurers, managed care organizations and others. Third-party payors are increasingly attempting to contain their costs. We cannot predict actions third-party payors may take, or whether they will limit the coverage and level of reimbursement for our products or refuse to provide any coverage at all. Reduced or partial reimbursement coverage could make our products less attractive to patients, suppliers and prescribing physicians and may not be adequate for us to maintain price levels sufficient to realize an appropriate return on our investment in our product candidates or compete on price.

In some cases, insurers and other healthcare payment organizations try to encourage the use of less expensive generic brands and over-the-counter, or OTC, products through their prescription benefits coverage and reimbursement policies. These organizations may make the generic alternative more attractive to the patient by providing different amounts of reimbursement so that the net cost of the generic product to the patient is less than the net cost of a prescription brand product. Aggressive pricing policies by our generic product competitors and the prescription benefits policies of insurers could have a negative effect on our product revenues and profitability.

Many managed care organizations negotiate the price of medical services and products and develop formularies for that purpose. Exclusion of a product from a formulary can lead to its sharply reduced usage in the managed care organization patient population. If our products are not included within an adequate number of formularies or adequate reimbursement levels are not provided, or if those policies increasingly favor generic or OTC products, our market share and gross margins could be negatively affected, as could our overall business and financial condition.

The competition among pharmaceutical companies to have their products approved for reimbursement may also result in downward pricing pressure in the industry or in the markets where our products will compete. We may not be successful in any efforts we take to mitigate the effect of a decline in average selling prices for our products. Any decline in our average selling prices would also reduce our gross margins.

In addition, managed care initiatives to control costs may influence primary care physicians to refer fewer patients to oncologists and other specialists. Reductions in these referrals could have a material adverse effect on the size of our potential market and increase costs to effectively promote our products.

We are subject to new legislation, regulatory proposals and managed care initiatives that may increase our costs of compliance and adversely affect our ability to market our products, obtain collaborators and raise capital.

There have been a number of legislative and regulatory proposals aimed at changing the healthcare system and pharmaceutical industry, including reductions in the cost of prescription products and changes in the levels at which consumers and healthcare providers are reimbursed for purchases of pharmaceutical products. For example, the Prescription Drug and Medicare Improvement Act of 2003 which was recently enacted. This legislation provides a new Medicare prescription drug benefit beginning in 2006 and mandates other reforms. Although we cannot predict the full effects on our business of the implementation of this new legislation, it is possible that the new benefit, which will be managed by private health insurers, pharmacy benefit managers and other managed care organizations, will result in decreased reimbursement for prescription drugs, which may further exacerbate industry-wide pressure to reduce the prices charged for prescription drugs. This could harm our ability to market our products and generate revenues. It is also possible that other proposals will be adopted. As a result of the new Medicare prescription drug benefit or any other proposals, we may determine to change our current manner of operation, provide additional benefits or change our contract arrangements, any of which could harm our ability to operate our business efficiently, obtain collaborators and raise capital.

We have only recently been relisted on the Nasdaq SmallCap Market and our stock is thinly traded and you may not be able to sell our stock when you want to do so.

From April 1999, when we were delisted from Nasdaq, until September 9, 2004, when we were relisted on the Nasdaq SmallCap Market, there was no established trading market for our common stock. During that time, our common stock was quoted on the OTC Bulletin Board and was thinly traded. There is no assurance that we will be able to comply with all of the listing requirements necessary to maintain relisted on the Nasdaq SmallCap Market. In addition, our stock remains thinly traded and you may be unable to sell our common stock during times when the trading market is limited.

The price of our common stock has been, and may continue to be, volatile.

The market price of our common stock, like that of the securities of many other development stage biotechnology companies, has fluctuated over a wide range and it is likely that the price of our common stock will fluctuate in the future. Over the past three years, the sale price for our common stock, as reported by Nasdaq and the OTC Bulletin Board has fluctuated from a low of $0.18 to a high of $10.07. The market price of our common stock could be impacted by a variety of factors, including:

- announcements of technological innovations or new commercial products by us or our competitors,
- disclosure of the results of pre-clinical testing and clinical trials by us or our competitors,
- disclosure of the results of regulatory proceedings,
- changes in government regulation,

- developments in the patents or other proprietary rights owned or licensed by us or our competitors,
- public concern as to the safety and efficacy of products developed by us or others,
- litigation, and
- general market conditions in our industry.

In addition, the stock market continues to experience extreme price and volume fluctuations. These fluctuations have especially affected the market price of many biotechnology companies. Such fluctuations have often been unrela