PRO PHARMACEUTICALS INC
Form 10-K
April 02, 2007
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

x Annual report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

For the fiscal year ended December 31, 2006

¨ Transition report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

For the transition period from to

Commission File No. 000-32877

PRO-PHARMACEUTICALS, INC.

Nevada	**04-3562325**
(State or other jurisdiction of incorporation)	**(I.R.S. Employer Identification No.)**
7 Wells Avenue, Newton, Massachusetts	**02459**
(Address of Principal Executive Offices)	**(Zip Code)**

(617) 559-0033

(Registrant s Telephone Number, Including Area Code)

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

Title of each class	Name of Exchange on which registered
Common Stock, Par Value $.001	American Stock Exchange

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

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ¨ NO x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. YES ¨ NO x

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 information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act.

Large accelerated filer ¨ Accelerated filer ¨ Non-accelerated filer x

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ¨ NO x

The aggregate market value of the voting and non-voting common equity held by non-affiliates computed by reference to the price at which the common equity was sold, or the average bid and asked price of such common equity, as of June 30, 2006 was $59,427,601.

The number of shares outstanding of the registrant s common stock as of March 22, 2007 was 40,364,793.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for the 2007 Annual Meeting of Stockholders are incorporated by reference into Part III of this Report.

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FOR THE FISCAL YEAR ENDED DECEMBER 31, 2006

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FORWARD-LOOKING STATEMENTS

This annual report on Form 10-K contains, in addition to historical information, forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on management s current expectations and are subject to a number of factors and uncertainties, which could cause actual results to differ materially from those described in such statements. We caution investors that actual results or business conditions may differ materially from those projected or suggested in forward-looking statements as a result of various factors including, but not limited to, the following: uncertainties as to the utility and market for our potential products; uncertainties associated with pre-clinical and clinical trials of our drug delivery candidates; our limited experience in product development and expected dependence on potential licensees and collaborators for commercial manufacturing, sales, distribution and marketing of our potential products; possible development by competitors of competing products and technologies; lack of assurance regarding patent and other protection of our proprietary technology; compliance with and change of government regulation of our activities, facilities and personnel; uncertainties as to the extent of reimbursement for our potential products by government and private health insurers; our dependence on key personnel; our history of operating losses and accumulated deficit; and economic conditions related to the biotechnology and biopharmaceutical industry. We cannot assure you that we have identified all the factors that create uncertainties. Readers should not place undue reliance on forward-looking statements.

Dollar amounts are presented in thousands throughout this document.

RESTATEMENT

Subsequent to the issuance of the 2005 consolidated financial statements, we determined that the common stock purchase warrants that were issued as part of our equity finance transactions in October 2003, April 2004 and August 2004, respectively, and which were accounted for in stockholders equity at their relative fair value upon issuance, should have been accounted for as derivative liabilities in accordance with Statement of Financial Accounting Standards (SFAS) No. 133, Accounting for Derivative Instruments and Hedging Activities. The warrants did not meet any of the scope exceptions allowed by SFAS 133. Specifically, the warrants did not meet the criteria in paragraph 11(a) of SFAS 133 that a contract should not be considered a derivative instrument if it is (1) indexed to its own stock and (2) classified in stockholders equity. The warrants, when classified as derivative liabilities are required to be initially recorded at fair value and to be marked to fair value at the end of each reporting period, which results in a non-cash charge or credit to other income and expense in our consolidated statement of operations.

The accompanying consolidated financial statements for the years ended December 31, 2005 and 2004 have been restated. See Note 14 to the consolidated financial statements. Additionally, selected consolidated financial data for the year ended December 31, 2003, as presented in Item 6, has been restated.

PART I

Item 1. *Business*

Corporate Formation

We were incorporated under Nevada law in January 2001. In May 2001, we acquired all of the outstanding common stock of a Massachusetts corporation engaged in a drug delivery development business. After the acquisition, we merged with the Massachusetts corporation and are the surviving corporation. In December 2003 we organized Pro-Pharmaceuticals Securities Corp. as a wholly-owned Delaware subsidiary, the sole purpose of which is to hold our cash and cash equivalents in a tax efficient manner.

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Our address is 7 Wells Avenue, Newton, Massachusetts 02459. Our telephone number is (617) 559-0033, our fax number is (617) 928-3450, our e-mail address is squeglia@pro-pharmaceuticals.com, and our website address is www.pro-pharmaceuticals.com. Our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q and any amendments thereto, are fully accessible on our website without charge.

Business of Pro-Pharmaceuticals

Overview

Pro-Pharmaceuticals is a development stage pharmaceutical company engaged in the discovery, development and commercialization of carbohydrate-based therapeutic compounds for advanced treatment of cancer, liver, microbial, cardiovascular and inflammatory diseases. Our initial focus is the development of a new generation of anti-cancer treatments using carbohydrate polymers with the intent of enhancing the safety and efficacy of chemotherapy agents. Our technology utilizes carbohydrates to increase efficacy and reduce toxicity of chemotherapeutic drugs; rescue drugs that were shelved for toxicity or half-life issues; increase the solubility of existing drugs, and develop carbohydrate polymers as new chemical entities.

The need to improve drug therapies, particularly anti-cancer agents, is significant and represents a large market opportunity. Chemotherapeutics in use today typically cause serious adverse side effects that dramatically decrease a patient s quality of life. DAVANAT®, our lead product candidate, may increase the efficacy and decrease the toxicity of current chemotherapies when used in combination with existing U.S. Food and Drug Administration (FDA)-approved cancer drugs. In combination with 5-Fluorouracil (5-FU) one of the most widely used chemotherapeutics in the world DAVANAT® has successfully completed a Phase I clinical trial for end-stage patients with all solid tumors and a Phase II trial for end-stage patients with metastatic colorectal cancer. We are currently dosing patients in two Phase II trials for first-line treatment of colorectal and biliary cancer. We have entered into a research collaboration with the Mount Sinai School of Medicine to evaluate the anti-fibrotic effects of one of our other novel carbohydrate compounds. All of our product candidates are in the development stage with one, DAVANAT®, in Phase II clinical trials.

Background on Carbohydrates

In order to function biologically, living organisms require the capability to recognize cellular information and trigger and perform biochemical reactions. Organisms as complex as human beings require systems with extraordinarily large capacity to recognize and translate information on a molecular level because of the tremendous number of different molecular messages that must be quickly and unambiguously deciphered, accepted or rejected. To accomplish this very important task, a class of molecules capable of great variation in shape, orientation and composition is required. Carbohydrates serve this function in the body because they have the large range of structural properties, including linkage variations, branching and anomeric isomers, that enables them to provide the significant recognition capabilities required. These complex molecules are also referred to as polysaccharides or complex sugars.

The particular role of carbohydrates, in this regard, is recognition of molecular information that triggers biological reactions. These activities include signal transmission, cell recognition, interaction and binding by other cells, hormones and viruses. Carbohydrates often accomplish this by working with lectins, which are carbohydrate binding proteins that exist on cells, and are not antibodies and have no enzymatic activity. Biological processes that involve lectin binding include a vast array of cell-cell interactions including infections, toxins and many physiological processes such as control and spread of metastasis.

In addition to their place in normal cell functioning, carbohydrates have been shown to play an important role in major diseases including cancer, cardiovascular disease, Alzheimer s disease, inflammatory disease and viral infections.

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Due to their structural complexity, which suits them for their cellular information transmission role, carbohydrates have not received as much scientific attention as nucleic acids and proteins and are not as well understood. We believe this offers a largely untapped area for treatment of disease including chemotherapeutics, infection treatment, vaccines and antibiotics. Our scientists have substantial expertise, developed over decades of study, in the area of carbohydrates that may enable us to efficiently develop successful products for disease treatment.

Drug Delivery Technologies and Importance for Cancer Treatment

The ultimate objective of enhanced drug delivery is to control and optimize localized application of the drug at the target site (location of disease) and rapidly eliminate from the body any amount not delivered to diseased tissue. Conventional drug delivery systems, such as controlled or sustained release, transdermal administration and others, are based on a physical erosion process for delivery of an active drug into the body over time with the objective of improving patient compliance with the therapy regimen. These systems do not address the need for site targeting, localized release or elimination of undelivered drug from the body all factors related to protection of healthy tissue from adverse or toxic effects of drugs.

The need for drug target delivery is widely recognized in the area of chemotherapy because the object of this treatment killing tumor cells is the factor that makes the treatment so toxic for healthy cells. Given the prominence of cancer as a disease, and the limitations of chemotherapy as a form of treatment, we selected chemotherapy drugs as the initial focus for our targeted delivery technology.

The limitations of these drugs create the opportunity for our target delivery technology. First, most chemotherapies kill cancer cells by disrupting cell division or formation, and hence are particularly damaging to growth and replication of the normal cells required by the body. The effect is most noticeable in fast-growing cells such as blood cells, digestive tract tissue, hair follicles, and reproductive organ cells. As a result, patients typically experience immediate and sometimes long-term decline in quality of life due to hair loss, nausea and other digestive problems, as well as anemia, fatigue, cardiovascular damage, and colon ulceration, among others.

Also, without the ability to target diseased tissue, chemotherapy is limited as a treatment by patient tolerance levels. Chemotherapy cannot always be administered in doses high enough to have optimal efficacy for disease reduction if the side effects to healthy tissue are too severe for patient recovery.

Business Strategy of Pro-Pharmaceuticals

Our objective is to discover, develop and commercialize carbohydrate-based therapeutic compounds for advanced treatment of cancer, liver, microbial, cardiovascular and inflammatory diseases. We foresee a market demand for target delivery of chemotherapy drugs that provide increased efficacy for treating cancer patients while reducing the toxic side effects of chemotherapy. Our initial focus is DAVANAT® is a non-toxic, target delivery technology based on a proprietary carbohydrate compound that we are combining with chemotherapy drugs that have been approved by the FDA and are widely used.

With respect to DAVANAT® in particular, our business objective is to develop it initially in combination with 5-FU and other chemotherapy drugs and biologics, and subsequently for other diseases, so that as a target delivery product it has broad application. Our clinical trial data to date in late stage patients shows that DAVANAT® keeps 5-FU in the blood stream substantially longer than 5-FU without DAVANAT® with no increase in key toxicity indicators. We are currently conducting clinical trials with first line colorectal and biliary cancer patients to demonstrate increased efficacy of DAVANAT® and to further support that this occurs with no increase in key toxicity indicators We plan to collaborate with pharmaceutical companies interested in improving compounds in these areas.

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Product Development

We are initially developing a pipeline of drug target delivery products that may be combined with FDA-approved and widely-used chemotherapies and biologics so as to increase their efficacy while reducing the toxic side effects. Based on our pre-clinical research, we believe DAVANAT®, when combined with approved and broadly marketed chemotherapies including irinotecan, doxorubicin, oxaliplatin, cisplatin, and bevacizumab (AVASTIN®) can significantly increase their clinical benefit.

We are developing other carbohydrate-based therapeutic compounds for treatment of other serious disease. These product candidates are all in the pre-clinical stage of development.

DAVANAT®

DAVANAT®, our lead product candidate in development, is a proprietary carbohydrate (polysaccharide) polymer comprised of mannose and galactose carbohydrates in a CARBOSOME formation. DAVANAT® is a complex polysaccharide derived from plant sources that has a precisely defined chemical structure. It is the galactomannan isolated from seeds of Cyamopsis Tetragonoloba, and subjected to a controlled partial chemical and physical degradation.

We believe the mechanism of action for DAVANAT® is based upon interaction with lectins, which are cell surface proteins that bind only to a particular kind of carbohydrate. DAVANAT® is formulated to attach to specific lectins (Galectins), which are abundant on the surface of tumor cells, while selectively avoiding healthy tissue. The galactose residue side chain attached to the carbohydrate polymer backbone targets lectin receptors that are specific and over-expressed on cancer cells. The receptor effectively interacts with the carbohydrate, chemotherapy drug combination and assists in the accumulation of the chemotherapy in the cancer cell, bypassing the normal defense mechanism. This form of targeted delivery may allow for administration of higher doses of chemotherapy thereby increasing efficacy while reducing toxicity.

Pre-clinical Studies of DAVANAT®

Our pre-clinical studies demonstrate that DAVANAT® when used in combination with 5-FU significantly reduces the toxicity of this widely-used chemotherapy. Pre-clinical studies also demonstrated delayed tumor growth and tumor shrinkage against a control group of animals when DAVANAT® was used with common combination therapies such as 5-FU/Leucovorin, 5-FU/Avastin®, and 5-FU/Irinotecan. These studies demonstrated not only that DAVANAT® enables increased efficacy of these chemotherapeutics, but also that it could be used effectively with several different chemotherapy drugs.

Clinical Trial Development of DAVANAT®

Phase I Trial for Third- and Fourth- Line Patients with Solid Tumors. In March 2005 we completed a Phase l study to evaluate DAVANAT® alone and in combination with 5-FU to treat solid tumors in a trial of 40 end-stage patients with advanced solid tumors who failed chemotherapy, radiation therapy, and/or surgical treatments. The open label study was designed to evaluate the safety and tolerability of escalating doses of DAVANAT® (30-280mg/m^2) when administered alone, and with a constant dose of 5-FU (500mg/m^2). The third-and fourth-line cancer patients when entering the study had advanced metastatic tumors that averaged more than 100mm, had progressive disease, and were refractory to chemotherapeutic agents including 5-FU.

Based on objective tumor assessment the disease was stabilized in 14 of 26 patients with measurable disease. Furthermore, 7 of 10 patients were stabilized at the highest dose level of DAVANAT® administered in the sixth and final cohort. Efficacy results are analyzed based on Response Evaluation Criteria in Solid Tumors (RECIST) following completion of the second cycle of treatment. RECIST defines stable disease as [n]either sufficient shrinkage to qualify for Partial Response (more than 30% shrinkage) nor sufficient increase to qualify for Progressive Disease (greater than 20% increase) taking as reference the smallest sum longest diameter since the treatment started.

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The Phase I data also indicate that DAVANAT®/5-FU was well tolerated by patients. The maximum tolerated dose was not reached indicating DAVANAT ®s safety and the potential for further dose escalation. Adverse side effects were mostly disease related. Additionally, the results showed that 5-FU, in combination with DAVANAT®, remained significantly longer in the bloodstream of cancer patients, potentially increasing 5-FU s efficacy with no increase in toxicity.

Phase II Trial for End Stage Patients with Third- and Fourth- Line Metastatic Colorectal Cancer. In 2004, we initiated a Phase II clinical trial to further evaluate DAVANAT®/5-FU for end-stage patients with third- and fourth-line metastatic colorectal cancer. This cancer is the fourth most commonly diagnosed cancer among men and women in the United States. The multi-center, open label, single-dose level study was designed to evaluate up to 15 patients in stage one, and up to 18 patients in stage two. The study, which was designed to evaluate the efficacy and safety of DAVANAT®/5-FU when administered at the same regimen as Phase I in monthly cycles, had two objectives: (1) to document the rate of response and stabilization of patients with advanced colon cancer; and (2) to continue evaluating the safety of the DAVANAT®/5-FU combination. Dosing of patients began in May 2005. We stopped recruiting for the study in May 2006 because we achieved our objective and saw no benefit to continue the study. We have replaced this study with two first line phase II trials to demonstrate the efficacy of DAVANAT®/5-FU in early stage patients. We closed the study in October 2006 and are currently summarizing the results. The unaudited data for the study indicate that based on objective tumor assessment one patient experienced a partial tumor response and the disease was stabilized in 6 of 20 patients. Again the study demonstrated the safety and tolerability of DAVANAT®/5-FU and showed that 5-FU, in combination with DAVANAT®, remains significantly longer in the bloodstream of cancer patients, potentially increasing 5-FU s efficacy with no increase in toxicity.

Phase II Trial for First-lineTreatment of Patients with Biliary Cancer. In 2005, we initiated a Phase ll trial for the first-line treatment of patients with biliary cancer. Biliary cancer may represent an opportunity for orphan drug status approval. See FDA Orphan Drug Designation below under Government Regulation. The multi-center, open label, single-dose level study is designed to evaluate up to 42 patients. The study, will evaluate the efficacy and safety of DAVANAT®/5-FU when administered for at least two monthly cycles or until disease progression. The trial has two objectives: (1) complete/partial tumor response in 20% of patients (17% in the first stage); and (2) the safety of DAVANAT®/5-FU regimen in this patient population. We currently have three sites recruiting patients and are adding additional sites in the U.S. and Europe.

Phase II Trial for First-line Patients with Colorectal Cancer. In November 2006, we initiated a Phase II trial for first-line treatment of colorectal cancer patients. The multi-center, open label, single-dose level study is designed to evaluate up to 50 patients who are unable to sustain the high toxicity of current intensive combination chemotherapy. The study, is expected to evaluate the efficacy and safety of DAVANAT®/5-FU when administered in combination with Leucovorin and AVASTIN® in two monthly cycles or until disease progression or toxicity. The primary objectives of the study are a complete or partial response in 33 percent of the patients and a secondary measurement of progression free survival at 6 and 12 months. We currently have six sites participating in the study and are adding additional sites.

Phase III Trial for Patients with Second-Line Colorectal Cancer. We initiated a Phase III trial for second-line treatment of patients with colorectal cancer. The multi-center, randomized, double blind study is designed to evaluate up to 100 patients. The study which is expected to evaluate the efficacy and safety of DAVANAT®/5-FU in administered in combination with Leucovorin and Oxaliplatin or Leucovorin and Irinotecan depending on what patients have received in first line therapy, in two monthly cycles or until disease progression. The study has the following objectives: progression free survival (six months), response rates, time to progression and quality of life. We currently have four sites and recruiting patients is on hold pending obtaining the financial resources to proceed with this trial.

Please see Risks Related to Pro-Pharmaceuticals Our Drug Candidates Are in Clinical Trials and Results Are Uncertain for additional discussion of risks related to clinical trials.

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Patents and Proprietary Rights

Patents and other intellectual property rights are essential to our business. Our success depends in part upon our continuing ability to file and maintain U. S. and foreign patents that adequately protect the intellectual property important to the development of our business.

We have been awarded 5 patents and have an additional 13 patent applications pending in the United States. In addition we have been awarded 14 foreign patents and have 27 foreign patent applications pending in various international jurisdictions. Further, we have 1 PCT (Paris Convention Treaty) patent application. Many of our patents and patent applications cover methods and composition for reducing toxicity and enhancing the delivery of a chemotherapeutic drug by co-administering a polysaccharide with a chemotherapeutic agent. Additionally, we have patent applications in a number of other areas related to utilizing carbohydrates to treat major disease.

We have also developed trade secrets and know-how. We require our employees, consultants and collaborators to enter into confidentiality agreements to protect our intellectual property. Please see Risks Related to Pro-Pharmaceuticals We Are a Counterclaim Defendant in a Lawsuit Instituted by CEO David Platt and Risks Related to the Drug Development Industry Our Competitive Position Depends on Protection of Our Intellectual Property for additional discussion of risks related to protection of our intellectual property based on inventions.

We have registered the following trademarks: PRO-PHARMACEUTICALS, INC., DAVANAT, and ADVANCING DRUGS THROUGH GLYCOSCIENCE. We filed applications to register additional trademarks and servicemarks.

Research

Our initial focus is on the design and analysis of carbohydrate-based compounds for targeted drug delivery. We contract with independent laboratories and accredited facilities to conduct our research, which is designed, evaluated and managed by our scientists. We do not anticipate building in-house research or development facilities or hiring staff in this connection other than for purposes of designing and managing our out-sourced research.

As we develop products eligible for clinical trials, we contract with independent parties to design the trial protocols, arrange for and monitor the clinical trials, collect data and analyze data. In addition, certain clinical trials for our products may be conducted by government-sponsored agencies and will be dependent on governmental participation and funding. Our dependence on independent parties and clinical sites involves risks including reduced control over the timing and other aspects of our clinical trials.

Our research and development expenditures totaled approximately $13.5 million for the cumulative period from inception (July 10, 2000) through December 31, 2006.

Manufacturing and Marketing

We are a development company at this time and do not intend to establish internal facilities for the manufacture of our products for clinical or commercial production. In order to have our products manufactured, we have developed and will continue to develop relationships with third-parties that have established manufacturing capabilities for the manufacture of our products on a contract basis.

Because our products are in the development stage, we have not created a sales and marketing staff to commercialize pharmaceutical products. If we develop products eligible for commercial sale, we will need to develop a sales and marketing capability or rely on third parties such as licensees, collaborators, joint venture partners or independent distributors to market and sell those products. Our dependence on third-party manufacturers and marketers will involve risks relating to our reduced control, and other risks including those discussed in Risk Factors Related to Pro-Pharmaceuticals Results We Will Depend on Third Parties To Manufacture and Market Our Products.

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Competition

A limited number of biotechnology and pharmaceutical companies are developing new drug delivery technologies for the treatment of cancer and other diseases. Drug delivery targeting technologies including monoclonal antibodies being developed by companies such as Seattle Genetics, Inc., Immunogen, Inc. and Dendreon Corporation could be competitive with our carbohydrate-based platforms. Several companies, including Momenta Pharmaceuticals, Inc., and GlycoFi, Inc., are developing carbohydrate technologies and sequencing of complex sugars to improve or develop new or existing drugs. Neose Technologies, Inc. is seeking to improve the therapeutic profile of widely used protein-based drugs and Optimer Pharmaceuticals, Inc. is developing carbohydrate technologies for drug discovery and improvement. While these companies may broaden the market for our products they may also provide competitive alternatives to our products.

Please see Risk Factors Related to the Drug Development Industry We Face Intense Competition in the Biotechnology and Pharmaceutical Industries for additional discussion related to our current and potential competition.

Government Regulation

The research, development, testing, manufacture, labeling, promotion, advertising, distribution, and marketing, among other things, of our products are extensively regulated by governmental authorities in the United States and other countries. In the United States, the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act and its implementing regulations. Failure to comply with the applicable U.S. requirements may subject us to administrative or judicial sanctions, such as FDA refusal to approve pending new drug applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, and/or criminal prosecution. Please see Risk Factors That May Affect Results We Will Need Regulatory Approvals To Commercialize Our Products for additional discussion of risks related to regulatory compliance.

Drug Approval Process

Drugs may not be marketed in the U.S. until the FDA has approved them. The steps required before a drug may be marketed in the U.S. include (similar rules apply in other countries):

1. Pre-clinical laboratory tests, animal studies, and formulation studies,

2. Submission to the FDA of an Investigational New Drug application (IND) for human clinical testing, which must become effective before human clinical trials may begin,

3. Adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for each indication,

4. Submission to the FDA of a New Drug Application (NDA),

5. Satisfactory completion of an FDA inspection of the manufacturing facility or facilities, at which the drug is produced to assess compliance with cGMP established by the FDA,

6. FDA review and approval of the NDA, and

7. FDA review and approval of a trademark used in connection with a pharmaceutical.

Pre-clinical tests include laboratory evaluation of product chemistry, toxicity, and formulation, as well as animal studies. The results of the pre-clinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before

that time the FDA raises concerns or questions about issues such as the conduct of the trials as outlined in the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. There is no certainty that submission of an IND will result in the FDA allowing clinical trials to begin.

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Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Each trial must be reviewed and approved by an independent Institutional Review Board (IRB) before it can begin. Study subjects must sign an informed consent form before participating in a clinical trial. Phase I usually involves the initial introduction of the investigational drug into people to evaluate its safety, dosage tolerance, pharmacodynamics, and, if possible, to gain an early indication of its effectiveness. Phase II usually involves trials in a limited patient population to (i) evaluate dosage tolerance and appropriate dosage; (ii) identify possible adverse effects and safety risks; and (iii) evaluate preliminarily the efficacy of the drug for specific indications. Phase III trials usually further evaluate clinical efficacy and test further for safety by using the drug in its final form in an expanded patient population. There is no assurance that these trials will be completed within a specified period of time, if at all.

Assuming successful completion of the required clinical testing, the results of the pre-clinical studies and of the clinical studies, together with other detailed information, including information on the manufacture and composition of the drug, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. Before approving an NDA, the FDA usually will inspect the facilities at which the drug is manufactured, and will not approve the product unless cGMP compliance is satisfactory. If the FDA evaluates the NDA and the manufacturing facilities as acceptable, the FDA will issue an approval letter. If the FDA evaluates the NDA submission or the manufacturing facilities as not acceptable, the FDA will outline the deficiencies in the submission and often will request additional testing or information. Even if an applicant submits the requested additional information, the FDA ultimately may decide that the NDA does not satisfy the regulatory criteria for approval. The testing and approval process requires substantial time, effort, and financial resources, and there is no assurance that any approval will be granted on a timely basis, if at all. After approval, certain changes to the approved product, such as adding new indications, manufacturing changes, or additional labeling claims are subject to further FDA review and approval.

Please see Risks Related to the Drug Development Industry We Will Need Regulatory Approvals to Commercialize Our Products for additional discussion of regulatory risks related to our drug development program.

FDA Fast Track Program; Priority Review

The FDA s fast track program is intended to facilitate the development and expedite the review of drugs intended for the treatment of serious or life-threatening diseases and that demonstrate the potential to address unmet medical needs for such conditions. Under this program, the FDA can, for example, review portions of an NDA for a fast track product before the entire application is complete, thus potentially beginning the review process at an earlier time. We may seek to have some of our products designated as fast track products, with the goal of reducing review time. There can be no guarantee that the FDA will grant any of our requests for fast track designation, that any fast track designation would affect the time of review, or that the FDA will approve the NDA submitted for any of our product candidates, whether or not fast track designation is granted. Additionally, FDA approval of a fast track product can include restrictions on the product s use or distribution (such as permitting use only for specified medical procedures or limiting distribution to physicians or facilities with special training or experience), and can be conditioned on the performance of additional clinical studies after approval.

FDA procedures also provide priority review of NDAs submitted for drugs that, compared to currently marketed products, offer a significant improvement in the treatment, diagnosis, or prevention of a disease. NDAs that are granted priority review are acted upon more quickly than NDAs given standard review. The FDA s goal

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is to act on 90% of priority NDAs within six months of receipt. We anticipate seeking priority review with regard to some of our product candidates. There can be no guarantee that the FDA will grant priority review status in any instance, that priority review status will affect the time of review, or that the FDA will approve the NDA submitted for any of our product candidates, whether or not priority review status is granted.

Post-Approval Requirements

If FDA approval of one or more of our products is obtained, we will be required to comply with a number of post-approval requirements. For example, holders of an approved NDA are required to report certain adverse reactions to the FDA and to comply with certain requirements concerning advertising and promotional labeling for their products. Also, quality control and manufacturing procedures must continue to conform to cGMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMP. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. In addition, discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA, including withdrawal of the product from the market. Also, new government requirements may be established that could delay or prevent regulatory approval of our products under development.

FDA Orphan Drug Designation

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which generally is a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are publicly disclosed by the FDA. Orphan drug designation does not convey an advantage in, or shorten the duration of, the regulatory review and approval process. If a product which has an orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to orphan exclusivity, meaning that the FDA may not approve any other applications to market the same drug for the same indication, except in certain very limited circumstances, for a period of seven years. As well, orphan drugs usually receive ten years of marketing exclusivity in the European Union.

Non-United States Regulation

Before our products can be marketed outside of the United States, they are subject to regulatory approval similar to that required in the United States, although the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary widely from country to country. No action can be taken to market any product in a country until an appropriate application has been approved by the regulatory authorities in that country. The current approval process varies from country to country, and the time spent in gaining approval varies from that required for FDA approval. In certain countries, the sales price of a product must also be approved. The pricing review period often begins after market approval is granted. No assurance can be given that even if a product is approved by a regulatory authority, satisfactory prices will be approved for such product.

Environmental Regulation

Pharmaceutical research and development involves the controlled use of hazardous materials. Biotechnology and pharmaceutical companies must comply with laws and regulations governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens and wastes. We do not anticipate building in-house research, development or manufacturing facilities, and, accordingly, do not expect to have to comply directly with environmental regulation. However, our contractors and others conducting research, development or manufacturing activities for us may be required to incur significant compliance costs, and this could in turn could increase our expense or delay our completion of research or manufacturing programs.

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Employees

As of March 2007, we had eight full-time employees, comprised of our President and Chief Executive Officer; Chief Financial Officer; Chief Operating Officer; Chief Scientist; Executive Vice President, Manufacturing and Product Development; Vice President of Investor Relations; Director of Clinical Trials; and an Operations Administrator. Our Medical Director and Monitor for our clinical trials provide services part-time as independent consultants.

Our executive officers are as follows:

Officers

David Platt, Ph.D. is the President, Chief Executive Officer, and Chairman of the Board of Directors. Dr. Platt is a co-founder of our Company and co-developer of our core technology. From March 1995 through May 2000, Dr. Platt was founder, CEO, and chairman of the Board of Directors of SafeScience Inc. subsequently known as GlycoGenesys, Inc. From 1992 to 1995, Dr. Platt was the CEO and chairman of the Board of Directors of International Gene Group, Inc. a company that he founded, took public in 1995, and is the predecessor company to SafeScience. Dr. Platt received a Ph.D. in chemistry in 1988 from The Hebrew University in Jerusalem. In 1989, Dr. Platt was a research fellow at the Weizmann Institute of Science, Rehovot, Israel, and from 1989 to 1991, was a research fellow at the Michigan Cancer Foundation (re-named Barbara Ann Karmanos Cancer Institute). From 1991 to 1992, Dr. Platt was a research scientist with the Department of Internal Medicine at the University of Michigan. Dr. Platt has published peer-reviewed articles and holds many patents, primarily in the field of carbohydrate chemistry.

Maureen E. Foley has served as the Chief Operating Officer of Pro-Pharmaceuticals since October 2001. Prior to that, she was Manager of Operations from January 2001 until October 2001. Ms. Foley has been involved in the start-up of several high tech companies, where she was responsible for the establishment and administration of business operations including human resources, benefits, accounting, finance, marketing, product development and project management. Her experience with start-up companies includes: From June 2000 to December 2000, she provided business operations services for eHealthDirect, Inc., a developer of medical records processing software. From October 1999 to May 2000, Ms. Foley managed business operations services for ArsDigita, Inc., a developer of business software and programs. From June 1996 to August 1999, Ms. Foley served with Thermo Fibergen, Inc., a subsidiary of Thermo Electron Corporation, a paper waste processing developer. She is a director and Chairman of Tax/Eze, Inc., a tax preparation and financial services company and a director of Stewart Precision Inc. Ms. Foley is a graduate of The Wyndham School, Boston, Massachusetts, with a major in Mechanical Engineering.

Carl L. Lueders, M.B.A., C.P.A., joined the management team in February 2005 as Chief Financial Officer. Mr. Lueders has a broad range of experience in finance, operations, short- and long-term planning, forecasting, performance measurement, SEC reporting, and controls. He was most recently Chief Financial Officer for R.F. Morse & Son, a privately held agri-based company. Previously, he was Interim Chief Executive Officer at Brine, a privately held manufacturer and distributor of sports equipment. Mr. Lueders spent 22 years with publicly held Polaroid in finance and planning roles, including Vice President and Controller, Treasurer and Acting Chief Financial Officer. Earlier in his career, Mr. Lueders was a Senior Auditor with Arthur Andersen. He is a C.P.A. and received his B.A. in Economics from the University of Massachusetts at Amherst and his M.B.A. from Babson College

Eliezer Zomer, Ph.D., is Executive Vice President of Manufacturing and Product Development. Prior to joining the company, Dr. Zomer had been the founder of Alicon Biological Control, where he served from November 2000 to July 2002. From December 1998 to July 2000, Dr. Zomer served as Vice President of product development at SafeScience, Inc. and Vice President of Research and Development at Charm Sciences, Inc. from June 1987 to November 1998. Dr. Zomer received a B.Sc. degree in industrial microbiology from the University of Tel Aviv in 1972, a Ph.D. in biochemistry from the University of Massachusetts in 1978, and undertook a post-doctoral study at the National Institute of Health.

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Our directors are as follows:

Directors

David Platt (see officers)

Dale H. Conaway, D.V.M., has served as a member of the Board of Directors since May 2001. Since 2001, Dr. Conaway has been the Deputy Regional Director (Southern Region) and Chief Veterinary Medical Officer for the Office of Research Oversight, an office within the Veterans Health Administration under the U.S. Department of Veterans Affairs. From 1998 to 2001, Dr. Conaway served as Manager of the Equine Drug Testing and Animal Disease Surveillance Laboratories for the Michigan Department of Agriculture. From 1994 to 1998, he was Regulatory Affairs Manager for the Michigan Department of Public Health Vaccine Production Division. Dr. Conaway received a D.V.M. degree from Tuskegee Institute and an M.S. degree in pathology from the College of Veterinary Medicine at Michigan State University.

Mildred S. Christian, Ph.D., has served as a member of the Board of Directors since October 2002. Dr. Christian is president and CEO of Argus International, Inc., a provider of consulting services in regulatory affairs, and Chairman and CEO of Argus Health Products, LLC, which develops and internationally distributes preventive and maintenance healthcare products for healthcare professionals and the over-the-counter market. Until 2002, Dr. Christian was Executive Director, Science and Compliance, of Charles River Laboratories and Primedica Corporation. Before founding Argus Research Laboratories in 1979 and Argus International in 1980, Dr. Christian spent 14 years in drug development at McNeil Laboratories, a division of Johnson & Johnson Corporation. She has participated at all levels in the performance, evaluation, and submission in more than 1,800 pre-clinical studies, from protocol to final report. Dr. Christian is a member of several professional organizations, including service as Councilor of the European Teratology Society and Secretary/Treasurer of the Academy of Toxicological Sciences, and was past president of the Teratology Society, the American College of Toxicology, and the Academy of Toxicological Sciences. Dr. Christian is an honorary member of the Society of Quality Assurance and founding editor of the Journal of Toxicological Sciences. She has edited or contributed to several major textbooks and is the author of more than 120 papers and abstracts published in U.S. and international journals. Dr. Christian earned her Ph.D. from Thomas Jefferson University in developmental anatomy and pharmacology.

Henry J. Esber, Ph.D., has served as a director since April 2006. From 2005 to present, Dr. Esber has been a Principal in Esber D&D consulting. From 2003 to 2005, Dr. Esber was a Senior Consultant, Business Development at Charles River Labs, Discovery and Development Services. From 2005 to 2006, Dr. Esber was a consultant and from 2006, he was Senior Vice President and Chief Business Officer for Bio-Quant. Dr. Esber is the co-founder of BioSignature Diagnostics, Inc. and Advanced Drug Delivery, Inc. He also serves on the Scientific Advisory Boards of several biotechnology companies and is the author of more than 130 technical publications. Dr. Esber has more than 25 years of experience in the areas of oncology/tumor immunology and immunotherapy as well as strong knowledge in the field of toxicology and regulatory affairs. Dr. Esber received a B.S. degree in biology/pre-med from the College of William and Mary, an M.S. degree in public health and parasitology from the University of North Carolina, and a Ph.D. in immunology/microbiology from West Virginia University Medical Center.

James T. Gourzis, M.D., Ph.D. Dr. Gourzis has served as a director since December 2006. Dr. Gourzis has extensive experience in formulating scientific and regulatory strategy and heading clinical development teams for pharmaceutical and biotechnology products, small molecules and biologics. Therapeutic area experience includes: oncology, cardiovascular, virology, immunology, central nervous system, allergy, anti-inflammatory, infectious disease, pain management and gastrointestinal disease. Dr. Gourzis is Principal, MEDRAND Associates from 2002 to present, providing consulting services with respect to scientific, strategic and regulatory considerations associated with the development of drugs and biologics. Previously, Dr. Gourzis held senior executive positions with bio-pharmaceutical companies: Senior Medical Director, PAREXEL International Corporation; Vice President Medical Affairs, Gensia Sicor (Teva) Pharmaceuticals; Chief Operating Officer, HiIl Top Pharmatest; Administrative Director, Group Health Associates; Executive Director Medical Research,

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Merrell-National Laboratories; and Senior Director Clinical Research, Schering Corporation. Dr. Gourzis received an A.B. degree in biology from Harvard University, an A.M. degree in pharmacology from Boston University and a Ph.D. in pharmacology/medicine from the University of Manitoba.

Steven Prelack has served as a director since April 2003. Since 2001, he has served as Senior Vice President, Chief Financial Officer and Treasurer of VelQuest Corporation, a provider of automated compliance management solutions for the pharmaceutical industry. In this capacity, Mr. Prelack oversees business development, financial, administrative and other functions, and is responsible for VelQuest s transition from a development-stage company to an operating company. From 1996 to 2000, he was Senior Vice President, Chief Financial Officer and Treasurer of LifeMetrix, Inc., a leading provider of cancer disease management services, as well as disease management technology, data and clinical trial product lines and related technology-based services. As co-founder of LifeMetrix, Mr. Prelack was responsible for all stages of its development, including initial seed capital funding, execution of its strategic business plan, and sale of the company. Mr. Prelack is a director of Codeco Corporation, a designer and manufacturer of custom resisters and switches, and of Sight Code, Inc., which specializes in OPM, a systems design and architecture platform. Mr. Prelack, a Certified Public Accountant, received a B.B.A. degree from the University of Massachusetts at Amherst in 1979.

Jerald K. Rome has served as a director since March 2004. He has been a private investor from 1996 to the present. Previously, Mr. Rome founded Amberline Pharmaceutical Care Corp., a marketer of non-prescription pharmaceuticals, in 1993 and served as its President from 1993 to 1996. From 1980 to 1990, he served as Chairman, President and Chief Executive Officer of Moore Medical Corp., a national distributor of branded pharmaceuticals and manufacturer and distributor of generic pharmaceuticals, and was previously Executive Vice President of the H.L. Moore Drug Exchange, a division of Parkway Distributors and predecessor of Moore Medical Corp. Mr. Rome received a B.S. degree in pharmaceutical sciences from the University of Connecticut.

Item 1A. ***Risk Factors***

An investment in our common stock involves a high degree of risk. You should carefully consider the risks described below and the other information before deciding to invest in our common stock. The risks described below are not the only ones facing our company. Additional risks not presently known to us or that we currently consider immaterial may also adversely affect our business. We have attempted to identify below the major factors that could cause differences between actual and planned or expected results, but we cannot assure you that we have identified all of those factors.

If any of the following risks actually happen, our business, financial condition and operating results could be materially adversely affected. In this case, the trading price of our common stock could decline, and you could lose all or part of your investment.

Risks Related to Pro-Pharmaceuticals (dollar amounts in thousands)

We Are at an Early Stage of Development with Limited Operating History. We are a development-stage company with a limited operating history, and we have not generated any revenues to date. We have no therapeutic products available for sale, and none are expected to be commercially available for several years, if at all. We may never generate revenue or become profitable, even if we are able to commercialize any products.

We Have Incurred Net Losses to Date and Depend on Outside Capital. Our accumulated deficit as of December 31, 2006 was $25,727. We will need to continue to conduct significant research, development, testing and regulatory compliance activities that, together with projected general and administrative expenses, we expect will result in substantial operating losses for the next several years. Accordingly, we do not expect to be generating sales or other revenue and will remain dependent on outside sources of financing during that time. If we are unable to raise funds from outside sources for our continuing operations, we may be adversely affected.

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We may raise such capital through public or private equity financings, partnerships, debt financings, bank borrowings, or other sources. Additional funding may not be available on favorable terms or at all. If adequate funds are not otherwise available, we may need to significantly curtail operations. To obtain additional funding, we may need to enter into arrangements that require us to relinquish rights to certain technologies, products and/or potential markets. To the extent that additional capital is raised through the sale of equity, or securities convertible into equity, our equity holders may experience dilution of their proportionate ownership of the company.

Based on $5,773 of available cash and cash equivalents and certificate of deposit as of December 31, 2006, we believe that we have sufficient capital to fund our operations through at least June 2007. We must raise cash before June 2007 or we may not be able to continue operations.

Our Product Candidates Are Based on Novel Unproven Technologies. Our product candidates are based on novel unproven technologies using proprietary carbohydrate compounds in combination with FDA approved of drugs currently used in the treatment of cancer and other diseases. Carbohydrates are difficult to synthesize, and we may not be able to synthesize carbohydrates that would be usable as delivery vehicles for the anti-cancer drugs we plan to work with.

Our Drug Candidates Are in Clinical Trials and Results Are Uncertain. We have one product candidate in human clinical trials. Pre-clinical results in animal studies are not necessarily predictive of outcomes in human clinical trials. Clinical trials are expensive, time-consuming and may not be successful. They involve the testing of potential therapeutic agents, or effective treatments, in humans, typically in three phases, to determine the safety and efficacy of the product candidates necessary for an approved drug. Many products in human clinical trials fail to demonstrate the desired safety and efficacy characteristics. Even if our products progress successfully through initial human testing, they may fail in later stages of development. We will be dependent on others to conduct our clinical trials, including clinical research organizations and, possibly, government-sponsored agencies. These trials may not start or be completed as we forecast, or may be unsuccessful.

Our Product Candidates May Not Be Successfully Commercialized. Even if our product candidates are successful in clinical trials, they may not be successfully commercialized. Potential products may fail to receive necessary regulatory approvals, be difficult to manufacture on a large scale, be uneconomical to produce, fail to achieve market acceptance, or be precluded from commercialization by proprietary rights of third parties.

Our Lack of Operating Experience May Cause Us Difficulty in Managing Our Growth. We have limited experience in manufacturing or procuring products in commercial quantities, conducting other later-stage phases of the regulatory approval process, selling pharmaceutical products, or negotiating, establishing and maintaining strategic relationships. Any growth of our company will require us to expand our management and our operational and financial systems and controls. If we are unable to do so, our business and financial condition would be materially harmed. If rapid growth occurs, it may strain our operational, managerial and financial resources.

We Will Depend on Third Parties to Manufacture and Market Our Products. We do not have, and do not now intend to develop, facilities for the manufacture of any of our products for clinical or commercial production. Accordingly, we will need to develop relationships with manufacturers and enter into collaborative arrangements with licensees or have others manufacture our products on a contract basis. We expect to depend on such collaborators to supply us with products manufactured in compliance with standards imposed by the FDA and foreign regulators.

In addition, we have limited experience in marketing, sales or distribution, and we do not intend to develop a sales and marketing infrastructure to commercialize our pharmaceutical products. If we develop commercial products, we will need to rely on licensees, collaborators, joint venture partners or independent distributors to market and sell those products.

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We Depend on Key Individuals to Develop Our Products and Pursue Collaborations. We are highly dependent on David Platt, Ph.D., President and Chief Executive Officer; Anatole Klyosov, Ph.D., our chief scientist; and Eliezer Zomer, Ph.D., Vice President, Manufacturing and Product Development. The loss of any of these persons, or failure to attract or retain other key personnel, could prevent us from pursuing collaborations or developing our products and core technologies.

We Are a Counterclaim Defendant in a Lawsuit Instituted by CEO David Platt. Our CEO David Platt filed a lawsuit in Massachusetts in January 2004 against GlycoGenesys, Inc. for claims including breach of contract. In its answer GlycoGenesys named us as a counterclaim defendant alleging tortious interference and misappropriation of proprietary rights, and seeks monetary damages and injunctive relief related to our intellectual property. In March 2004, we answered the counterclaim and denied any liability. We and Dr. Platt intent to contest these counterclaims vigorously. In October 2006, pursuant to a U.S. Bankruptcy Court approval of a liquidation of GlycoGenesys Marlborough Research and Development, Inc. (now known as Prospect Therapeutics, Inc) purchased selected assets of GlycoGenesys including this litigation. If we do not prevail there could be a material adverse impact on our financial position, results of operations or cash flows.

Risks Related to the Drug Development Industry

We Will Need Regulatory Approvals to Commercialize Our Products. We currently do not have products approved for sale in the U.S. or any foreign market. We are required to obtain approval from the FDA in order to sell our products in the U.S. and from foreign regulatory authorities in order to sell our products in other countries. The FDA s review and approval process is lengthy, expensive and uncertain. Extensive pre-clinical and clinical data and supporting information must be submitted to the FDA for each indication for each product candidate in order to secure FDA approval. The FDA could reject an application or require us to conduct additional clinical or other studies as part of the regulatory review process. Delays in obtaining or failure to obtain FDA approvals would prevent or delay the commercialization of our products, which would prevent, defer or decrease our receipt of revenues. If we receive initial regulatory approval, our product candidates will be subject to extensive and rigorous ongoing domestic and foreign government regulation.

Our Competitive Position Depends on Protection of Our Intellectual Property. Development and protection of our intellectual property are critical to our business. If we do not adequately protect our intellectual property, competitors may be able to practice our technologies. Our success depends in part on our ability to obtain patent protection for our products or processes in the United States and other countries, protect trade secrets, and prevent others from infringing on our proprietary rights.

Since patent applications in the United States are maintained in secrecy for at least portions of their pendency periods (published on U.S. patent issuance or, if earlier, 18 months from earliest filing date for most applications) and since other publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain that we are the first to make the inventions to be covered by our patent applications. The patent position of biopharmaceutical firms generally is highly uncertain and involves complex legal and factual questions. The U.S. Patent and Trademark Office has not established a consistent policy regarding the breadth of claims that it will allow in biotechnology patents.

We cannot assure you that all of our patent applications will issue as patents or that the claims of any issued patents will afford meaningful protection for our technologies or products. In addition, patents issued to us or our licensors may be challenged and subsequently narrowed, invalidated or circumvented. Patent litigation is widespread in the biotechnology industry and could harm our business. Litigation might be necessary to protect our patent position or to determine the scope and validity of third-party proprietary rights, and we may not have the required resources to pursue such litigation or to protect our patent rights.

Although we require our scientific and technical employees and consultants to enter into broad assignment of inventions agreements, and all of our employees, consultants and corporate partners with access to proprietary information to enter into confidentiality agreements, these agreements may not be honored.

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We are a counterclaim defendant in a lawsuit instituted by Dr. Platt. See Risks Related to Pro-Pharmaceuticals above.

Products We Develop Could Be Subject to Infringement Claims Asserted by Others. We cannot assure that products based on our patents or intellectual property that we license from others will not be challenged by a third party claiming infringement of its proprietary rights. If we were not able to successfully defend our patents or licensed rights, we may have to pay substantial damages, possibly including treble damages, for past infringement.

We Face Intense Competition in The Biotechnology and Pharmaceutical Industries. The biotechnology and pharmaceutical industries are intensely competitive. We face direct competition from U.S. and foreign companies focusing on drug delivery technologies, which are rapidly evolving. Our competitors include major, multinational pharmaceutical and chemical companies, specialized biotechnology firms and universities and other research institutions. Many of these competitors have greater financial and other resources, larger research and development staffs and more effective marketing and manufacturing organizations, than we do. In addition, academic and government institutions are increasingly likely to enter into exclusive licensing agreements with commercial enterprises, including our competitors, to market commercial products based on technology developed at such institutions. Our competitors may succeed in developing or licensing technologies and products that are more effective or less costly than ours, or succeed in obtaining FDA or other regulatory approvals for product candidates before we do.

Health Care Cost Containment Initiatives and the Growth of Managed Care May Limit Our Returns. Our ability to commercialize our products successfully will be affected by the ongoing efforts of governmental and third-party payors to contain the cost of health care. These entities are challenging prices of health care products and services, denying or limiting coverage and reimbursement amounts for new therapeutic products, and for FDA-approved products considered experimental or investigational, or which are used for disease indications without FDA marketing approval.

Even if we succeed in bringing any products to the market, they may not be considered cost-effective and third-party reimbursement might not be available or sufficient. If adequate third-party coverage is not available, we may not be able to maintain price levels sufficient to realize an appropriate return on our investment in research and product development. In addition, legislation and regulations affecting the pricing of pharmaceuticals may change in ways adverse to us before or after any of our proposed products are approved for marketing.

Our Insurance Coverage May Not Be Adequate In All Circumstances. In the future, we may, in the ordinary course of business, be subject to claims by, and liability to, persons alleging injury as a result of taking products we have under development. If we are successful in having products approved by the FDA, the sale of such products would expose us to additional potential product liability and other claims resulting from their use. This liability may result from claims made directly by consumers or by pharmaceutical companies or others selling such products. Although we currently have insurance coverage for both product liability and professional liability, it is possible that we will not be able to maintain such insurance on acceptable terms. Any inability to maintain insurance coverage on acceptable terms could prevent or limit the commercialization of any products we develop.

Risks Related to Our Stock

Stock Prices for Biopharmaceutical and Biotechnology Companies Are Volatile. The market price for securities of biopharmaceutical and biotechnology companies historically has been highly volatile, and the market from time-to-time has experienced significant price and volume fluctuations that are unrelated to the operating performance of such companies. Fluctuations in the trading price or liquidity of our common stock may adversely affect our ability to raise capital through future equity financings.

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Large Sales Could Reduce the Trading Price of our Common Stock. Listed on the American Stock Exchange since September 2003, our common stock, despite certain increases of trading volume from time to time, experiences periods when it could be considered thinly traded. On March 21, 2007, we issued approximately 5.2 million shares to discharge approximately $3.9 million of $4.4 million outstanding obligations under our 7% Convertible Debentures. We issued the shares at a discount to the then trading price of our stock. Although resale of these shares will be subject to the volume limitations of Rule 144 under the Securities Act (as they are restricted securities), the former Debenture holders and warrant holders may attempt to resell them as rapidly as Rule 144 permits. Such sales could place downward pressure on the trading price of our stock.

We May Need to Undertake Finance Transactions with Persons Who May Not Intend to Become Long-Term Investors. Our recent equity finance transactions were structured as a so-called PIPE (private investment in public equity). In general, these transactions attract purchasers who desire to buy securities at a discount to the trading price that may be profitably and rapidly resold into the public markets after the privately placed securities are registered. Rapid resales of stock and other factors related to these transactions often exert a downward pressure on the trading price of a stock. We may find, given our present stage of development, that we must undertake this type of finance transaction in the future.

Four Principal Stockholders Own Enough Shares to Control The Company. Four of our principal stockholders, David Platt, James Czirr, Offer Binder and Anatole Klyosov own or control approximately 31% of the outstanding shares of our common stock, and Dr. Platt and Mr. Czirr together own approximately 25%. Some or all of these stockholders, acting in concert, may be able to substantially influence the election of the Board of Directors and other corporate actions requiring stockholder approval, such as recapitalization or other fundamental corporate action, as well as the direction and policies of our company. Such concentration of ownership also could have the effect of delaying, deterring or preventing a change in control of the company that might otherwise be beneficial to stockholders.

Changes in Laws, Regulations and Financial Accounting Standards May Affect Our Reported Results of Operations. The Sarbanes-Oxley Act of 2002 and related regulations may result in changes in accounting standards or accepted practices within our industry and could add significant new costs to being a public company. New laws, regulations and accounting standards, as well as changes to currently accepted accounting practices, could adversely affect our reported financial results and negatively affect our stock price. Additional unanticipated expenses incurred to comp