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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

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**FORM 10-K**

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

For the fiscal year ended December 31, 2005

**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

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**PRO-PHARMACEUTICALS, INC.**

Nevada  
(State or other jurisdiction  
of incorporation)

189 Wells Avenue, Newton, Massachusetts  
(Address of Principal Executive Offices)

04-3562325  
(I.R.S. Employer  
Identification No.)

02459  
(Zip Code)

(617) 559-0033

(Registrant's Telephone Number, Including Area Code)

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

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

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

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  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

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

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, 2005 was \$46,134,080.

The number of shares outstanding of the registrant's common stock as of March 10, 2006 was 27,315,411.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the definitive Proxy Statement for the 2006 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, 2005**

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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.

### PART I

#### Item 1. *Business*

##### Corporate Formation

We were incorporated under Nevada law in January 2001. On May 15, 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.

Our address is 189 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](mailto:squeglia@pro-pharmaceuticals.com), and our website address is [www.pro-pharmaceuticals.com](http://www.pro-pharmaceuticals.com). Our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q are fully accessible on our website without charge.

##### Business of Pro-Pharmaceuticals

###### *Overview*

Pro-Pharmaceuticals is a development stage company engaged in the discovery, development and commercialization of carbohydrate-based therapeutic compounds. We believe our expertise in carbohydrates offers numerous opportunities to provide advanced treatment of disease including cancer, cardiovascular disease, inflammatory, liver and microbial disease and viral infections.

Our work has initially concentrated on target delivery of chemotherapy drugs for the treatment of cancer. We believe our lead product candidate in this area, — DAVANAT<sup>®</sup> — when used in combination with existing U.S. Food and Drug Administration (FDA) approved cancer drugs may increase the efficacy and decrease the toxicity of current chemotherapy treatment.

DAVANAT<sup>®</sup> in combination with 5-Fluorouracil (5-FU), a widely used chemotherapy, has successfully completed a Phase I human clinical trial and is currently in a Phase II human clinical trial. We have also

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undertaken pre-clinical work with DAVANAT® in combination with other chemotherapy drugs and have evidence that DAVANAT® works effectively with a wide range of approved chemotherapy drugs. 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.

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 technologies. 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

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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.

Second, 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***

We plan to focus on commercializing DAVANAT<sup>®</sup> before developing other carbohydrate product candidates.

We foresee a market demand for target delivery of chemotherapy drugs that provide increased efficacy for treating cancer tumors while reducing the toxic side effects of chemotherapy. Additionally, we believe commercialization of DAVANAT<sup>®</sup> may occur within a shorter period of time and at lower cost than most other new drug approvals. This is because DAVANAT<sup>®</sup> is not a new drug. DAVANAT<sup>®</sup> is a non-toxic target delivery technology based on a proprietary carbohydrate compound that we are combining with chemotherapy drugs that have already been approved by the FDA and are already widely used.

With respect to DAVANAT<sup>®</sup> in particular, our business objective is to develop it initially in combination with 5-FU and other chemotherapy drugs, and subsequently for other diseases, so that as a target delivery product it has broad application. We will seek to obtain definitive clinical data before engaging others to assist us with commercialization. Commercialization may be in the form of direct distribution, sales and marketing agreements, out-licensing, or partnership with a pharmaceutical company. We plan to apply this approach in the United States as well as major international markets.

### ***Product Development***

We are initially developing a pipeline of drug delivery products that may be combined with FDA-approved and widely-used chemotherapies so as to increase their efficacy while reducing the toxic side effects. Based on our research, we believe we can combine DAVANAT<sup>®</sup>, with a number of other established and broadly marketed chemotherapies including irinotecan, doxorubicin, paclitaxel, oxaliplatin, cisplatin, and bevacizumab (AVASTIN<sup>®</sup>).

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

### **DAVANAT<sup>®</sup>**

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

We believe DAVANAT<sup>®</sup>'s mechanism of action is based upon interaction with lectins, which are cell surface proteins that bind only to a particular kind of carbohydrate. DAVANAT<sup>®</sup> is formulated to attach to lectins, on the surface of tumor cells, while selectively avoiding healthy tissue. The galactose residue side chain attached to the carbohydrate polymer backbone targets a lectin receptor that is specific and over-expressed on cancer cells. The receptor effectively pulls the carbohydrate compound — chemotherapy drug combination — into the cancer cell, bypassing the normal defense mechanism. If the carbohydrate compound and chemotherapy drug combination is not absorbed by a lectin it is secreted from the body. This form of targeted delivery may allow for higher doses of chemotherapy administration with reduced 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 against a control group of animals when DAVANAT® was used in combination with 5-FU and Leucovorin, 5-FU and Avastin®, and Irinotecan. These studies demonstrated not only that DAVANAT® enables increased efficacy, 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 I study to evaluate DAVANAT® alone and in combination with 5-FU to treat solid tumors in a trial of 40 patients with advanced solid malignancies 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<sup>2</sup>) when administered alone, and with a constant dose of 5-FU (500mg/m<sup>2</sup>). The third- and fourth-line cancer patients when entering the study had solid tumors that averaged more than 100mm, had progressive disease, and were refractory to all chemotherapeutic treatments including 5-FU.

Based on objective tumor assessment the disease was stabilized in 14 of 26 patients with measurable disease. Seven of ten patients were stabilized at the highest dose level 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.”

The Phase I data also indicate that DAVANAT®/5-FU was well tolerated by patients. There were no serious adverse side effects associated with DAVANAT®. Additionally, the results showed that 5-FU, in combination with DAVANAT®, remains significantly longer in the bloodstream of cancer patients, potentially increasing 5-FU’s efficacy while lowering toxicity.

- *Phase II Trial for Patients with Third- and Fourth- Line Metastatic Colorectal Cancer.* In 2004, we initiated a Phase II clinical trial to evaluate DAVANAT®/5-FU for 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 is designed to evaluate up to 15 patients in stage one, and up to 18 patients in stage two. The study, which is expected to evaluate the efficacy and safety of DAVANAT®/5-FU when administered in six monthly cycles, has two objectives: (1) to document the rate of response and stabilization of the disease; and (2) to evaluate the compound’s safety. Dosing of patients began in May 2005. We have completed enrollment in the first stage of this trial and expect to report results in the second quarter of 2006.

In September 2005, we initiated a Phase II trial for the first-line treatment of cholangiocarcinoma (cancer of the bile duct). Cholangiocarcinoma currently has no standard of care and may represent an opportunity for orphan drug status approval. See “FDA ‘Orphan Drug’ Designation” below under “Government Regulation.” We also received clearance from the EMEA (European Medicines Agency) to initiate a Phase III study for the second line treatment of metastatic colorectal cancer of DAVANAT®/5-FU in combination with other chemotherapy drugs. We are evaluating the protocols for these two trials and expect to begin dosing of at least one of these trials in the second quarter of 2006. We may initiate additional clinical trials in 2006 to evaluate the efficacy of DAVANAT® in combination with chemotherapy drugs.

### ***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.

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We have 5 patents and 12 patent applications pending in the United States. In addition we have 19 foreign patents and 14 foreign patent applications pending in various jurisdictions. Further we have 8 PCT (Paris Convention Treaty) patent applications pending. 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.

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 clinical research organizations (CRO) to design the trial protocols and arrange for and monitor the clinical trials. We also rely on academic institutions or clinical research organizations to conduct, supervise or monitor some or all aspects of clinical trials involving our products. 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 CRO's involves risks including reduced control over the timing and other aspects of our clinical trials.

Our research and development expenditures totaled approximately \$10.5 million for the cumulative period from inception (July 10, 2000) through December 31, 2005.

### ***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 That May Affect Future Results — We Will Depend On Third Parties To Manufacture And Market Our Products."

### ***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

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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 That May Affect Future Results — 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.

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.

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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.

### *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 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

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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.

### *Employees*

As of March 2006, we had seven 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; and an Operations Administrator. Our Medical Director/Monitor for the clinical trials provides service part-time as an independent consultant.

### **Scientific Advisory Board**

Our Scientific Advisory Board includes recognized scientists with expertise in the fields of carbohydrate chemistry and biochemistry, immunology, cell and molecular biology, and synthetic and medical chemistry. The board members work with management to identify scientific and product development opportunities and to review the progress of specific projects.

*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, he was founder, CEO, and chairman of the Board of Directors of SafeScience Inc. now 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 of Jerusalem, Israel. In 1989, Dr. Platt was a research fellow in 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.

*Anatole A. Klyosov, Ph.D., D.Sc.* is a co-founder of the Company, Chief Scientist and a co-inventor of our patented technology. From 1996 to 2005 Dr. Klyosov was vice president, research and development for Kadant Composites, Inc., a subsidiary of Kadant, Inc., where he directed a laboratory performing work in biochemistry, microbiology, polymer engineering, and other fields in the development of composite polymer-based products. From 1990 to 1998, Dr. Klyosov was visiting professor of biochemistry, Center for Biochemical and Biophysical Sciences, Harvard Medical School, and from 1981 to 1990 he was professor and head of the Carbohydrates Research Laboratory at the A.N. Bach Institute of Biochemistry, USSR National Academy of Sciences. Dr. Klyosov was elected as a member of the World Academy of Art and Sciences and is the recipient of several distinguished awards including the USSR National Award in Science and Technology. He has published more than 200 peer-reviewed articles in scientific journals, authored books on enzymes, carbohydrates, and biotechnology, and holds more than 20 patents. Dr. Klyosov has consulted for numerous organizations, including the World Bank and the United Nations Industrial Development Organization, and serves on the editorial boards of scientific journals in the field of biochemistry and biotechnology. Dr. Klyosov earned his Ph.D. and D.Sc. degrees in physical chemistry, and an M.S. degree in enzyme kinetics, from Moscow State University.

*Dale H. Conaway, D.V.M.*, has served as a member of the Board of Directors since May 2001. Dr. Conaway is 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, he 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.

*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.

*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

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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 of research of Argus and Redfield Laboratories, both divisions of Charles River Laboratories. 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 over 1,800 pre-clinical studies, from protocol to final report. Dr. Christian is a member of 20 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. She 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 over 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.

*Edgar Ben-Josef, M.D.*, is associate professor, Department of Radiation Oncology, at the University of Michigan Medical School and previously had been associate professor (2000 to 2003) and assistant professor (1995 to 2000) in radiation oncology at Wayne State University School of Medicine. Since 1995, Dr. Ben-Josef has served as an attending physician at the Gershenson Radiation Oncology Center, Karmanos Cancer Institute, in Detroit, Michigan. Dr. Ben-Josef received B.Med.Sc. and M.D. degrees from The Hebrew University-Hadassah School of Medicine in Jerusalem, Israel. He also is a member of our Medical Advisory Board and a former member of our Board of Directors.

*Henry J. Esber, Ph.D.*, is a senior consultant, business development, at Charles River Laboratories. He 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.

*Irwin Goldstein, Ph.D.*, is Emeritus Professor and Interim Chair of the Department of Biological Chemistry at the University of Michigan Medical School, and was Professor from 1972 to 1999. Dr. Goldstein is the recipient of many professional awards and is the author of more than 200 publications. Dr. Goldstein received a B.A. degree in chemistry from Syracuse University, and a Ph.D. in biochemistry from the University of Minnesota.

*Zbigniew J. Witczak, Ph.D.*, is associate professor at the Nesbitt School of Pharmacy, Wilkes University (Wilkes-Barre, Pennsylvania). From 1991 to 1999, Dr. Witczak was associate professor in the Department of Pharmaceutical Studies, School of Pharmacy, at the University of Connecticut. Dr. Witczak has extensive industrial and academic experience in carbohydrates. In 2002, he chaired the Division of Carbohydrate Chemistry of the American Chemical Society (ACS) and was the chair of its awards committee. He has published more than 80 research papers and holds patents in the field of carbohydrate, medicinal and biological chemistry, and serves on the editorial board of numerous journals in carbohydrate chemistry and related fields. In 1997, Dr. Witczak co-edited *Carbohydrates in Drug Design*, which has since become a leading reference in the field. In 2000, Dr. Witczak was awarded the Melville L. Wolform Award of the ACS for his outstanding research contribution to carbohydrate chemistry. Dr. Witczak received a M.S. degree in organic chemistry from the University of Lodz and a Ph.D. in organic chemistry from the Faculty of Pharmacy, Medical University, Lodz, Poland. He worked as a postdoctoral fellow with Professor Roy L. Whistler, a renowned authority in carbohydrate chemistry at Purdue University.

### **Medical Advisory Board**

Our Medical Advisory Board includes recognized doctors with expertise in the area of clinical trial management. The Members assist management in the oversight of protocol development and management of our clinical trials.

*Edgar Ben-Josef, M.D. (see biography, Scientific Advisory Board)*

*Adi Kurgan, M.D., Ph.D.*, has 30 years of academic and medical experience and is board certified in General Surgery. Dr. Kurgan teaches and practices at The Hebrew University Hadassah Medical School and Shaare Zedek Hospital, Jerusalem. Dr. Kurgan is founder of community medical centers in Israel and participates in clinical research and medical device validation. He is the author of more than 40 clinical articles.

*Leslie R. Laufman, M.D.*, has 30 years of medical practice and clinical research experience, primarily in the areas of hematology and oncology. Board-certified in internal medicine, Dr. Laufman has served as a principal investigator for the Columbus (Ohio) Community Clinical Oncology Program, an investigator for the Ohio State University Comprehensive Cancer Center, and president of Hematology Oncology Consultants. Dr. Laufman is the author of more than 40 articles on oncology research and studies.

*John S. Macdonald, M.D.*, was professor of medicine at New York Medical College (New York City), and chief of gastrointestinal oncology service at Saint Vincent's Comprehensive Cancer Center (New York City). Dr. Macdonald was the recipient of the fifth annual Petros A. Palandjian Visiting Professor in Gastrointestinal Oncology Award at the Dana Farber Cancer Institute at Harvard in 2002. Dr. Macdonald is active in various cancer organizations and an editor or a member of the editorial advisory boards of numerous cancer publications and is the chief medical officer at Aptium. Dr. Macdonald is the author of more than 300 articles and has presented more than 130 abstracts in the oncology field.

*Bruce Silver, M.D., F.A.C.P.*, has 20 years of clinical oncology practice. Dr. Silver is a Board-certified medical oncologist, Fellow of the American College of Physicians, and member of the American Society of Clinical Oncology. Dr. Silver has participated in clinical trials for the treatment of breast, colon, ovary, lung cancers, lymphomas and Hodgkin's disease, and supportive care trials. He has served as chairman of the Cancer Committee and Tumor Boards and as a principal investigator at various hospitals. Dr. Silver is involved in providing oncology drug development consultative services to biotechnology and pharmaceutical clients and in the direct medical and safety management of these trials. Dr. Silver is senior director, global product development services for PRA International.

### **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.

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***We Have Incurred Net Losses to Date and Depend on Outside Capital.*** Our accumulated deficit as of December 31, 2005 was \$26,430. 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 will not 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.

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 \$4,466 of available cash and cash equivalents as of December 31, 2005, and approximately \$9.3 million of net proceeds raised through issuance of Convertible Debentures on February 14, 2006 we believe that we have sufficient capital to fund our operations through at least June 2007.

***Our Product Candidates Will Be Based on Novel Unproven Technologies.*** Our product candidates will be based on novel unproven technologies using proprietary carbohydrate compounds in combination with FDA approved 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.

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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.

***We Depend on Key Individuals to Develop Our Products and Pursue Collaborations.*** We are highly dependent on Dr. David Platt, President and Chief Executive Officer; Dr. Anatole Klyosov, our chief scientist; and Dr. Eliezer Zomer, 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 Dr. Platt.*** Dr. 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 intend to contest these counterclaims vigorously. If we do not prevail there could be a material adverse impact on our financial position, results of operations or cash flows.

***We Could Be Required to Make Substantial Cash Payments Upon an Event of Default Under Our Debentures.*** Our 7% Convertible Debentures provide for events of default including, without limitation, failure to timely make payments of principal, interest or other amounts due thereunder, failure to observe or perform any covenant or agreement set forth in the Debentures or other material agreements to which we are a party, default on another credit agreement or facility evidencing of obligations in excess of \$250, ineligibility of our stock for listing on quotation on a trading market, lapse of effectiveness of the registration statement registering the shares subject to this prospectus or inability of selling stockholders to offer and sell shares thereunder in excess of certain “blackout” periods, and failure to have the shares registered within 180 days after the February 14, 2006 date of sale of the Debentures and warrants. If an event of default occurs, the outstanding principal, plus accrued and unpaid interest due thereon, and all other amounts due under each Debenture may become, at the holder’s election, immediately due and payable in cash in an amount that is not less than the sum of (i) 130% of the outstanding principal plus accrued and unpaid interest and (ii) other amounts due to such holder. We would not be able to repay this amount without raising additional capital. Please see “Description of Transaction” below for additional detail about the Debentures and warrants.

***We Cannot Take Certain Actions Without the Consent of the Debenture Holders.*** For as long as at least \$1 million of our 7% Convertible Debentures remains outstanding, we cannot take certain actions, including, among others, incurrence of indebtedness beyond a stated amount, amendments of our charter or governance documents, repurchase or other acquisition of more than a de minimis number of the shares of our common stock or securities exercisable, convertible or exchangeable for shares of our common stock. These negative covenants may limit actions, such as a finance transaction that requires an amendment of our certificate of organization, that we believe are in the best interests of Pro-Pharmaceuticals but which we cannot complete if the holders of the Debentures do not consent.

### **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

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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.

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

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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.

***Large Sales Could Reduce the Trading Price of Our Common Stock.*** We listed our common stock on the American Stock Exchange in September 2003, prior to which our stock traded on the OTC Bulletin Board. Based on varying trading volume to date, our stock could be considered “thinly traded.” In 2003 and 2004, on behalf of existing stockholders, we registered for re-sale approximately 14.65 million shares of our common stock, and approximately 3.61 million shares of stock issuable upon exercise of immediately exercisable warrants. On behalf of the holders of our 7% Convertible Debentures and common stock purchase warrants, we are registering an additional 7.3 million shares of common stock issuable upon conversion or redemption of, or as interest payments on, the Debentures and exercise of the warrants. The interest and principal are payable monthly commencing July 1, and August 1, 2006, respectively, in shares of common stock, subject to some restrictions. In general, shares of registered common stock may be re-sold into the public markets without volume or other restrictions. Large sales of our registered shares could place substantial downward pressure on the trading price of our common stock, particularly if the amount sold significantly exceeds the then-current trading volume of our stock.

***Downward Pressure on Our Stock Price Could Result if Certain Stockholders Become Short-term Investors.*** Provided we meet certain requirements, all outstanding principal and interest under the Debentures may be paid in shares of our common stock. Within 6 months after issuance, the warrants we concurrently sold become exercisable. In connection with the sale of these securities, we agreed to promptly register the shares of our common stock issuable under the Debentures, and upon exercise of the warrant, for re-sale into the public markets. We may enter into similar financing transactions in the future with the same or different investors. Because such investors typically receive registered shares well in advance of the expiration of the holding periods under Rule 144 of the Securities Act, they may choose to sell their shares after a short period of holding our stock. If sufficient quantities of stock are sold during a brief interval of time, this could result in downward pressure on the market price for shares of our publicly traded common stock.

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**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 42% of the outstanding shares of our common stock, and Dr. Platt and Mr. Czirr together own approximately 34%. 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, including the expensing of stock options, could adversely affect our reported financial results and negatively affect our stock price. Additional unanticipated expenses incurred to comply with new requirements could also negatively impact our results of operations.

### **Item 1B. Unresolved Staff Comments**

None.

### **Item 2. Properties**

We entered into a five-year sublease that commenced on June 1, 2001 for approximately 2,830 square feet for our executive offices located at 189 Wells Avenue, Suite 200, Newton, Massachusetts 02459. The base rent for the year ended December 31, 2005 was approximately \$110,000. The sublease is a so-called "triple net" lease, meaning that we must pay our proportionate share of items such as property taxes, insurance and operating costs. In connection with the lease we have issued a letter of credit which is secured by restricted cash on deposit with the bank as a security deposit in the amount of \$21,933 which is renewed annually. During 2005, there were no capital expenditures related to our leased premises. Our sublease expires in May of 2006. We are actively seeking to obtain new leased space and expect to secure suitable leased facilities and complete a move prior to the expiration of our current sublease.

### **Item 3. Legal Proceedings**

In January 2004, Dr. Platt, our Chairman and Chief Executive Officer, filed a lawsuit in Massachusetts Superior Court against GlycoGenesys, Inc. for various claims including breach of contract. In its filing in February 2004, GlycoGenesys asserted counterclaims against us and Dr. Platt alleging tortious interference and misappropriation of proprietary rights. The counterclaims seek monetary damages and injunctive relief related to our intellectual property. In March 2004, we and Dr. Platt answered the counterclaims and denied any liability. In June 2004, the Court allowed, without opposition, a motion of GlycoGenesys for leave to file a supplemental counterclaim against us for defamation and unfair competition. We and Dr. Platt intend to contest these counterclaims vigorously and believe we will ultimately prevail. However, if we do not prevail, there could be a material adverse impact on our financial position, results of operations or cash flows. On February 2, 2006, GlycoGenesys filed a voluntary petition in bankruptcy for protection under Chapter 11 of the U.S. Bankruptcy Code, as a result of which the counterclaim litigation is stayed.

Pursuant to Board approval, we agreed to indemnify Dr. Platt for the expenses of his defense of the counterclaims, some of which may be recoverable under insurance. In 2005, we incurred \$259 of expenses in connection with this defense. Through December 31, 2005, we have incurred cumulative expenses of approximately \$427 in connection with this defense. No amount, if any, potentially recoverable from the insurance company has been recorded at December 31, 2005.

On January 28, 2005, we filed a request with the U.S. Patent and Trademark Office (USPTO) for an inter partes re-examination of U.S. Patent No. 6,680,306 owned by GlycoGenesys, Inc. because we believe that the

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invention claimed in this patent is anticipated by other inventions (technically, “prior art”), including our U.S. Patent No. 6,645,946 for DAVANAT®. In an October 18, 2005 action, the USPTO agreed with our argument that all claims stated in the ‘306 patent are anticipated by prior art. On December 19, 2005, GlycoGenesys filed a response to the USPTO, and on January 18, 2006 we responded to the GlycoGenesys submission. The matter is now before the USPTO for a final decision. We believe that the USPTO actions to date support our belief that the invention claimed in our DAVANAT patent is prior art relative to the GlycoGenesys patent.

#### **Item 4. *Submission of Matters to a Vote of Security Holders***

No matter was submitted to a vote of our stockholders during the fourth quarter of the fiscal year covered by this report.

**PART II****Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities****Price Range of Common Stock**

Our common stock trades under the symbol "PRW" on the American Stock Exchange. The high and low closing prices for our common stock as reported on the American Stock Exchange for the periods indicated below were as follows:

	<u>High</u>	<u>Low</u>
<b>Fiscal Year Ended December 31, 2005</b>		
First Quarter	\$2.97	\$2.40
Second Quarter	\$3.22	\$2.28
Third Quarter	\$3.09	\$2.59
Fourth Quarter	\$3.05	\$2.40
<b>Fiscal Year Ended December 31, 2004</b>		
First Quarter	\$5.51	\$3.75
Second Quarter	\$4.41	\$3.15
Third Quarter	\$4.04	\$2.08
Fourth Quarter	\$2.50	\$1.39

**Holder of Common Stock**

As of February 7, 2006, there were approximately 285 holders of record of our common stock. Because shares of our common stock are held by depositaries, brokers and other nominees, the number of beneficial holders of our shares is substantially larger than the number of record holders. Based on information available to us, we believe there are approximately 2,570 beneficial owners of our shares of our common stock in addition to the record holders.

**Dividends**

There have been no cash dividends declared on our common stock since our company was formed. Dividends are declared at the sole discretion of our Board of Directors. Our intention is not to declare cash dividends and retain all cash for our operations.

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**Item 6. Selected Consolidated Financial Data (in thousands except share and per share data)**

The following table sets forth financial data for the years ended December 31, 2005, 2004, 2003, 2002, and 2001 for the cumulative period since inception (July 10, 2000) through December 31, 2005. This selected financial data should be read in conjunction with the Consolidated Financial Statements and related notes included in Item 15 of this Annual Report on Form 10-K.

	Fiscal Year Ended December 31,					Cumulative Period from Inception (July 10, 2000) to December 31, 2005
	2005	2004	2003	2002	2001	
<b>Consolidated Statements of Operations Data:</b>						
Operating expenses:						
Research and development	\$ 3,040	\$ 3,042	\$ 1,950	\$ 1,483	\$ 893	\$ 10,509
General and administrative	3,615	4,262	2,988	1,804	1,289	14,024
Operating loss	(6,655)	(7,304)	(4,938)	(3,287)	(2,182)	(24,533)
Interest and other income	111	124	69	24	25	354
Interest and other expenses (1)			(4)	(415)	(1,813)	(2,251)
Net loss	\$ (6,544)	\$ (7,180)	\$ (4,873)	\$ (3,678)	\$ (3,970)	\$ (26,430)
Net loss per share:						
basic and diluted	\$ (0.24)	\$ (0.28)	\$ (0.23)	\$ (0.22)	\$ (0.29)	
Weighted average shares out-standing:						
basic and diluted (2)	27,315,411	25,750,789	21,360,572	16,374,524	13,601,795	

As of December 31,

	As of December 31,				
	2005	2004	2003	2002	2001
(dollars in thousands)					
<b>Consolidated Balance Sheet Data:</b>					
Working capital	\$ 3,314	\$ 9,819	\$ 7,318	\$ 1,327	\$ 1,021
Total assets	4,963	11,110	8,002	2,283	1,767
Convertible notes payable	—	—	—	—	195
Stockholders' equity	3,583	10,105	7,624	1,616	1,216

- (1) Interest expense in 2001 includes \$1,241 relating to a beneficial conversion feature and \$503 relating to the fair value of certain warrants issued to induce conversion of the notes prior to maturity.
- (2) Basic and diluted net loss per share is the same for each reporting period as the anti-dilutive shares were not included in the per-share calculations.
- (3) Amounts in this table may not agree due to rounding.

**Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations (in thousands, except share and per share data)**

**Overview**

We are a development-stage company engaged in research and development of carbohydrate based therapeutic compounds. We believe our carbohydrate-based compounds offer numerous opportunities to provide advanced disease treatments. Our initial focus is on the target delivery of chemotherapy drugs for the treatment of cancer. We believe our initial carbohydrate compound — DAVANAT® — may increase the body's tolerance to these toxic drugs by targeting the delivery directly to cancerous cells and increasing the efficacy, thereby creating a preferable treatment to existing oncology regimens. For additional information, please see "Item 1. Business — Business of Pro-Pharmaceuticals."

All of our drug candidates are currently in preclinical and clinical development. We currently have only one drug candidate — DAVANAT® — in clinical development. In general, in order to commercialize our current and future drug candidates, we are required to successfully complete preclinical studies and clinical trials and obtain regulatory approvals. Current requirements for regulatory approval include:

- preclinical toxicology, pharmacology and metabolism studies, as well as in-vivo efficacy studies in relevant animal models of disease;
- manufacturing of drug product for use in preclinical studies and clinical trials and ultimately for commercial supply;
- submission of the results of preclinical studies and information regarding manufacturing and control and proposed clinical protocol to the U.S. Food and Drug Administration (FDA) in an investigational new drug application (IND), or similar filings with regulatory agencies outside the United States;
- conduct of clinical trials designed to provide data and information regarding the safety and efficacy of the product candidate in humans; and
- submission of all the results of testing to the FDA in a new drug application (NDA), or similar filings with regulatory agencies outside the United States.

Upon approval by the appropriate regulatory authorities we may commence commercial marketing and distribution of the product. This process typically takes several years to complete and requires the expenditure of substantial resources. Any delay in obtaining or failure to obtain required approvals will materially adversely affect our ability to generate revenues from commercial sales relating to our drug candidates. We do not expect to file an NDA for a drug candidate before 2007. We anticipate our source of funding for the next several years to come from either financing transactions or collaborations with other pharmaceutical companies.

We are devoting substantially all of our efforts toward product research and development, and raising capital. We have no source of revenue and have incurred significant losses to date. We have incurred net losses of \$26,430 for the cumulative period from inception (July 10, 2000) through December 31, 2005. Our losses have resulted principally from costs associated with research and development expenses, including clinical trial costs, and general and administrative activities. As a result of planned expenditures for future research, discovery, development and commercialization activities, we expect to incur additional operating losses for the foreseeable future.

We have raised \$26,630 in capital principally through the issuance of convertible notes, the sale of common stock through a public offering and the sale of common stock and warrants through private placements as of December 31, 2005. From inception (July 10, 2000) through December 31, 2005, we used cash of \$21,483 for our operations. At December 31, 2005, we had \$4,466 of cash and cash equivalents available to fund future operations, which when combined with \$10,000 (approximately \$9.3 million net of transaction costs) we raised through the issuance of convertible debentures and warrants on February 14, 2006, we believe is sufficient to fund our operations through at least June 2007.

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Because we lack revenue and must continue our research and development, we must continually identify new sources of capital and complete financing transactions in order to continue our business. We must continually monitor the monthly “burn rate” of our capital resources.

### **Critical Accounting Policies and Estimates**

Our significant accounting policies are more fully described in Note 2 to our Consolidated Financial Statements included in this Annual Report on Form 10-K. Certain of our accounting policies, however, are critical to the portrayal of our financial position and results of operations and require the application of significant judgment by our management, which subjects them to an inherent degree of uncertainty. In applying our accounting policies, our management uses its best judgment to determine the appropriate assumptions to be used in the determination of certain estimates. Those estimates are based on our historical experience, terms of existing contracts, our observance of trends in the industry, information available from other outside sources, and on various other factors that we believe to be appropriate under the circumstances. We believe that the critical accounting policies discussed below involve more complex management judgment due to the sensitivity of the methods, assumptions and estimates necessary in determining the related asset, liability, revenue and expense amounts.

*Accrued Expenses.* As part of the process of preparing our financial statements, we are required to estimate accrued expenses. This process involves identifying services that third parties have performed on our behalf and estimating the level of service performed and the associated cost incurred on these services as of each balance sheet date in our financial statements. Examples of estimated accrued expenses include contract service fees, such as amounts paid to clinical research organizations (CRO) and investigators in conjunction with pre-clinical and clinical trials, professional service fees, such as those arising from the services of attorneys and accountants and accrued payroll expenses. In connection with these service fees, our estimates are most affected by our understanding of the status and timing of services provided relative to the actual services incurred by the service providers. In the event that we do not identify certain costs that have been incurred or we under- or over-estimate the level of services or costs of such services, our reported expenses for a reporting period could be understated or overstated. The date on which certain services commence, the level of services performed on or before a given date, and the cost of services are often subject to our judgment. We make these judgments based upon the facts and circumstances known to us in accordance with accounting principles generally accepted in the United States.

*Income Taxes.* We determine if our deferred tax assets and liabilities are realizable on an ongoing basis by assessing our valuation allowance and by adjusting the amount of such allowance, as necessary. At this time our primary deferred tax asset relates to our net operating loss carryforwards. In the determination of the valuation allowance, we have considered future taxable income and the feasibility of tax planning initiatives. Should we determine that it is more likely than not that we will realize certain of our deferred tax assets for which we previously provided a valuation allowance, an adjustment would be required to reduce the existing valuation allowance. In addition, we operate within multiple taxing jurisdictions and are subject to audit in these jurisdictions. These audits can involve complex issues, which may require an extended period of time for resolution. Although we believe that adequate consideration has been made for such issues, there is the possibility that the ultimate resolution of such issues could have an adverse effect on the results of our operations.

*Stock-Based Compensation.* We account for stock-based compensation to employees and non-employee directors in accordance with Accounting Principles Board (APB) Opinion No. 25, “Accounting for Stock Issued to Employees”, and related interpretations. Under APB No. 25, no compensation expense is recorded for stock options and restricted stock awards granted at fair market value with fixed terms. We account for stock or other equity-based compensation to non-employees utilizing the fair value method in accordance with Statement of Financial Accounting Standards (SFAS) No. 123, “Accounting for Stock-Based Compensation,” and the Emerging Issues Task Force Abstract No. 96-18, “Accounting for Equity Instruments that Are Issued to Other than Employees for Acquiring, or in Conjunction with, Selling Goods or Services,” and the related interpretations. Under the fair value method, compensation is recorded at the fair value of the consideration

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received or the fair value of the equity instrument until the final measurement date, which is the earlier of performance completion or vesting. Fluctuations in the quoted market price of the our stock covered by the unvested equity instrument are reflected as adjustments to deferred compensation and compensation expense over the related service period.

We determine the fair value of the equity instrument by using the Black-Scholes option-pricing model, which requires us to make certain assumptions. Some of the assumptions, such as the risk-free interest rate, come from published sources. Other assumptions, such as the expected life of the equity instrument or the expected volatility of our stock, are subjective and may differ from period to period. Accordingly, changes in the value of our stock or changes in the assumptions used to calculate the fair value of the equity instruments, such as the expected life of the options, could have a significant effect on our results of operations in any period.

We consider equity compensation to be an important component in attracting and retaining key employees. During 2005 and 2004, we awarded approximately 207,000 and 252,750 stock options, respectively, to employees and non-employee members of our Board of Directors for normal services. Because the exercise price of the options granted equal the fair market value of a share of our common stock on the date of grant and the options have fixed terms, we recorded no stock compensation expense on these awards. If we had used the fair value method provided for under SFAS No. 123 our reported net loss of \$6,544 would have increased by \$287 to \$6,831 in 2005.

In December 2004, the Financial Accounting Standards Board issued SFAS No. 123(R), "Share-Based Payment" (SFAS 123R). This Statement is a revision of SFAS No. 123, "Accounting for Stock-Based Compensation," and supersedes Accounting Principles Board Opinion No. 25, "Accounting for Stock Issued to Employees," and its related implementation guidance. SFAS 123R requires that we measure the grant date fair value of equity awards given to employees in exchange for services and recognize that cost over the period that such services are performed. We adopted SFAS 123R on January 1, 2006, using the modified-prospective transition method. Adoption of SFAS 123R will materially increase our stock compensation expense, net loss and net loss per share; it will not, however, have an impact on our financial position. For fiscal 2006, total stock-based compensation expense, including amounts from stock options using the fair value provisions of SFAS 123R, is estimated to be approximately \$155. In order to develop the fiscal 2006 stock-based compensation expense estimate, we utilized assumptions, including, among other items, expected life and volatility, which reflect assumptions used in 2005. Total unrecognized stock-based compensation expense related to unvested stock options and unvested restricted stock awards, expected to be recognized over a weighted average period of 2 years, amounted to \$159 at December 31, 2005. The amounts reflected above represent the unamortized value of existing option grants at December 31, 2005. While it is likely that stock options will be granted in 2006, no estimate of 2006 grants has been included in the 2006 estimate of stock based compensation expense.

## **Results of Operations**

### ***Fiscal Year Ended December 31, 2005 Compared to Fiscal Year Ended December 31, 2004 (in thousands)***

**Research and Development Expenses.** Research and development expenses were \$3,040 during the year ended December 31, 2005 as compared to \$3,042 incurred during the year ended December 31, 2004. We generally categorize research and development expenses as either direct external expense, comprised of amounts paid to third party vendors for services, or all other expenses, comprised of employee payroll and general overhead allocable to research and development. We subdivide external expenses between clinical programs and preclinical activities. We consider a clinical program to have begun upon acceptance by the FDA, or similar agency outside of the United States, to commence a clinical trial in humans, at which time we begin tracking expenditures by the product candidate. We have one product candidate — DAVANAT® — in clinical trials at this time. Clinical program expenses comprise payments to vendors related to preparation for, and conduct of, all phases of the clinical trial, including costs for drug manufacture, patient dosing and monitoring, data collection and management, oversight of the trials and reports of results. Pre-clinical expenses comprise all research and development amounts incurred before human trials begin, including payments to vendors for services related to

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product experiments and discovery, toxicology, pharmacology, metabolism and efficacy studies, as well as manufacturing process development for a drug candidate.

Our research and development expenses for the twelve months ended December 31, 2005 as compared to the twelve months ended December 31, 2004 were as follows:

	Twelve Months Ended December 31,	
	2005	2004
Direct external expenses		
Clinical programs	\$ 1,557	\$ 1,168
Pre-clinical activities	959	1,389
All other research and development expenses	524	485
	<u>\$ 3,040</u>	<u>\$ 3,042</u>

In summary, research and development expense in 2005 shifted from pre-clinical activities to clinical programs. The increase in clinical trial expense was due to the start-up and costs associated with the Phase II trial. We completed dosing patients in a Phase I clinical trial of DAVANAT<sup>®</sup> in March of 2005 and began dosing patients in a Phase II clinical trial of DAVANAT<sup>®</sup> in May of 2005 while the pre-clinical tests and experiments associated with DAVANAT<sup>®</sup> diminished in 2005 as compared to 2004.

In September 2005 we submitted an IND to the FDA for an additional Phase II clinical trial of DAVANAT<sup>®</sup>/5-FU to treat line one cholangiocarcinoma (cancer of the bile duct) patients. We also received clearance from the EMEA (European Medical Association) to begin a Phase III Colon Cancer trial of DAVANAT<sup>®</sup>/5-FU in combination with other chemotherapy drugs. These trials are designed to test the efficacy of DAVANAT<sup>®</sup> as a drug delivery compound for specific cancer indications and/or in combination with chemotherapeutic drugs. Further, on January 1, 2006 we added a Chief Scientist to our staff. We expect that these new clinical trials and the addition of our Chief Scientist will cause our research and development expenses to increase in 2006.

Both the time required and costs we may incur in order to commercialize a drug candidate that would result in material net cash inflow are subject to numerous variables, and hence we are unable at this stage of our development to forecast useful estimates. Variables that make estimates difficult include the number of clinical trials we may undertake, the number of patients needed to participate in the clinical trial, patient recruitment uncertainties, trial results as to the safety and efficacy of our product, and uncertainties as to the regulatory agency response to our trial data prior to receipt of marketing approval. Moreover, the FDA or other regulatory agencies may suspend clinical trials if we or an agency believes patients in the trial are subject to unacceptable risks, or find deficiencies in the conduct of the clinical trial. Delays or rejections may also occur if governmental regulation or policy changes during our clinical trials or in the course of review of our clinical data. Please see "Risks Related to Pro-Pharmaceuticals" and "Risks Related to the Drug Development Industry" for additional risks and other factors that make estimates difficult at this time. Due to these uncertainties, accurate and meaningful estimates of the ultimate cost to bring a product to market, the timing of costs and completion of our program and the period during which material net cash inflows will commence are unavailable at this time.

*General and Administrative Expenses.* General and administrative expenses were \$3,615 in 2005 or a decrease of 15%, as compared to \$4,262 in 2004. General and administrative expenses consist primarily of salaries, including stock based compensation, legal and accounting fees, insurance, investor relations, business development and other office related costs. The \$646 reduction in expense in 2005, consisted of a reduction in legal expense of approximately \$700. This was offset by an increase in payroll of approximately \$135 and a decrease in all other spending of approximately \$85. Of the \$700 decrease in legal expenses approximately \$560 was due to the patent arbitration between Dr. Platt, our CEO and GlycoGenesys which was conducted and completed in 2004. The arbitration concerned the rights to control prosecution of some patent applications that

Dr. Platt licensed to GlycoGenesys. In November 2004, the arbitrator awarded the patent prosecution rights to Dr. Platt. The remainder of the decrease in legal expenses as compared to 2004 was related to expenses incurred in 2004 to defend a lawsuit asserted by a former employee. This matter was concluded in 2004. These expense decreases were offset in part by an increase of approximately \$190 associated with legal expenses to defend the counterclaim lawsuit filed by GlycoGenesys against us and Dr. Platt as described in “Item 3 — Legal Proceedings” above.

We expect general and administrative costs to increase somewhat due to the implementation of SFAS No. 123R which will require us to begin expensing employee stock options in the first quarter of 2006. Additionally, spending may increase due to increased business development activity, ongoing compliance with the Sarbanes Oxley Act of 2002 and higher rent associated with finding new leased space to replace our existing expiring space lease.

*Interest and Other Income.* Interest and other income in 2005 was \$111 or a decrease of 10% as compared to \$124 in 2004. Interest and other income consists primarily of interest income on interest-bearing cash equivalents. The decrease in interest income is due to lower average cash balances partially offset by higher average interest rates. Average interest rates were approximately 1.42% per annum in 2005 versus approximately 1.30% per annum in 2004. Our interest expense will increase in 2006 as result of a \$10,000 Convertible Debenture which we issued on February 14, 2006. The Convertible Debenture carries interest at 7% per annum. The interest may be payable in Common Stock subject to certain provisions. The Convertible Debenture also includes 50% warrant coverage, and we expect the deemed fair value of such warrants, once determined, will be recorded as a debt discount, and such discount will be amortized as additional non cash interest expense.

***Fiscal Year Ended December 31, 2004 Compared to Fiscal Year Ended December 31, 2003 (in thousands)***

*Research and Development Expenses.* Research and development expenses were \$3,042 in 2004 or an increase of 56% as compared to \$1,950 incurred in 2003. Research and development expenses consist primarily of costs of clinical research organizations (CRO), clinical data management services, outsourcing product development to chemical research laboratories regulatory and medical consultants, drug manufacturing for clinical trials, salaries, stock based compensation and other personnel related expenses. Of the \$1,092 increase, approximately \$380 was due to Phase I clinical trials of DAVANAT®/5-FU and the remainder was due to drug manufacturing for clinical trials, pre-clinical product development and CRO costs primarily for Phase II clinical trials.

We began our Phase I clinical trial of DAVANAT® and DAVANAT®/5-FU in February 2003. Due to additional drug administration cycles, enrollment closed in January 2005. We completed the sixth and final cohort of the Phase I trial in March 2005.

*General and Administrative Expenses.* General and administrative expenses were \$4,262 in 2004 or an increase of 43%, as compared to \$2,988 in 2003. General and administrative expenses consist primarily of salaries, including stock based compensation, legal and accounting fees, insurance, investor relations, business development and other office related costs. Of the \$1,274 increase in costs in 2004, approximately \$1,315 was due to higher legal fees offset by lower expenses in other areas. Approximately \$580 of the legal fee increase was incurred in connection with the arbitration between GlycoGenesys, Inc. and David Platt concerning rights to control prosecution of some patent applications that Dr. Platt licensed to GlycoGenesys. In November 2004 the arbitrator awarded the patent prosecution rights to Dr. Platt. We consider the costs incurred on this matter to be ordinary and necessary for purposes of protection of our intellectual property in general and to enable us to defend the claims against our intellectual property alleged by GlycoGenesys described in “Item 3 — Legal Proceedings” above. The remainder of the increase in legal costs was incurred principally for the protection of our intellectual property. Legal expenses in 2004 also increased to a lesser degree by expenditures to defend the lawsuit asserted by a former employee.

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Additionally, investor relations expense increased by approximately \$135 in 2004. This increase was offset by lower stock-based compensation expense of approximately \$325. The lower stock-based compensation expense was primarily due to fewer compensatory option grants.

*Interest and Other Income.* Interest and other income in 2004 was \$124 or an increase of 80% as compared to \$69 in 2003. Interest and other income consists primarily of interest income on interest-bearing cash equivalents. The increase in interest income is due to higher average cash balances resulting from larger financings in 2004, partially offset by lower average interest rates. Average interest rates were approximately 1.30% per annum in 2004 versus approximately 1.60% per annum in 2003.

### **Liquidity and Capital Resources (in thousands)**

As described above in the section entitled “Overview” above and elsewhere in this Annual Report on Form 10-K, we are in the development stage and have not generated any revenues to date. Since our inception on July 10, 2000, we have financed our operations primarily through private placements of convertible debt, shares of common stock and warrants, and a public offering of shares of common stock. At December 31, 2005, we had raised a total of \$26,630 from these offerings and had \$4,466 of cash available. On February 14, 2006 we raised \$10,000 resulting in net proceeds after transaction costs of approximately \$9.3 million by issuing 7% Convertible Debentures and common stock warrants through a private placement. The Convertible Debentures and related interest may be repaid in common stock subject to certain provisions. The details of this transaction are more fully described in Note 11 (Subsequent Events) to our audited financial statements included with this annual report.

Net cash used in operations was \$6,127 in 2005 and \$6,333 in 2004. The decreased use of cash in operations in 2005 as compared to 2004 was primarily due to lower legal expenses incurred in 2004 associated with litigation matters that were resolved in 2004, offset in part by a lower rate of growth in current liabilities in 2005. We expect our cash needs to increase in 2006 to fund clinical trials and the addition of our Chief Scientist.

Net cash used in operations was \$6,333 in 2004 and \$4,152 in 2003 or an increase of \$2,181. The increase in 2004 was due to the impact of a full year’s research and management costs for the Phase I clinical trial of approximately \$380, drug manufacturing for clinical trials, pre-clinical product development and CRO costs primarily for Phase II clinical trials of approximately \$695, and higher legal costs related primarily to the patent arbitration and intellectual property litigation, described in “Item 3 — Legal Proceedings” above, of approximately \$1,315.

Net cash used in investing activities was approximately \$111 in 2005, \$69 in 2004 and \$105 in 2003. The increase in 2005 as compared to 2004 was due to increased patent costs related to DAVANAT® and other carbohydrate based compounds. Of the \$69 used in 2004 approximately \$46 was related to new patents and the remainder was related to furniture and equipment for office expansion. Fixed asset purchases were higher in 2003 as we added staff. We expect patent costs to remain flat in 2006 and capital expenditures to increase as a result of relocating our office when our lease expires in May of 2006.

Net cash provided by financing activities was zero in 2005, \$9,498 in 2004, \$9,944 in 2003. Net cash provided by financing activities in 2004 resulted from the sale of common stock and warrants through two private equity offerings, structured as “PIPE” transactions (Private Investment in Public Equity). In 2003, the net cash provided by financing activities resulted from the sale of common stock and warrants in three private placements with net proceeds of \$9,944.

We believe that our cash on hand of \$4,466 at December 31, 2005 when combined with the approximately \$9.3 million of net proceeds we raised on February 14, 2006 through the issuance of 7% Convertible Debentures will be sufficient to enable us to meet our financing and operating obligations through at least June 2007. We will require more cash to fund our operations and believe that we will be able to obtain additional financing. However, there can be no assurance that we will be successful in obtaining such new financing or, if available, that such financing will be obtainable on terms favorable to us.

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### **Payments Due Under Contractual Obligations (in thousands)**

The following table summarizes the payments due under our contractual obligations at December 31, 2005, and the effect such obligations are expected to have on liquidity and cash flow in future periods:

<u>Contractual Obligations</u>	<u>Payments due by period</u>				
	<u>Total</u>	<u>Less than 1 year</u>	<u>1 - 3 years</u>	<u>3 - 5 years</u>	<u>More than 5 years</u>
Contract with 30-day cancellation requirement	\$ 40	\$ 40	\$ —	\$ —	\$ —
Operating leases	69	59	10	—	—
<b>Total Payments Due Under Contractual Obligations</b>	<b>\$109</b>	<b>\$ 99</b>	<b>\$ 10</b>	<b>\$ —</b>	<b>\$ —</b>

On February 14, 2006 we issued \$10,000 of 7% Convertible Debentures due February 14, 2008. Under the terms of the Convertible Debentures, interest is payable monthly commencing July 1, 2006 and the outstanding principal is payable in 18 equal monthly installments commencing August 1, 2006. Payments may be made in Common Stock or cash at our option subject to certain restrictions.

### **Off-Balance Sheet Arrangements**

We have not created, and are not a party to, any special-purpose or off-balance sheet entities for the purpose of raising capital, incurring debt or operating parts of our business that are not consolidated into our financial statements. We do not have any arrangements or relationships with entities that are not consolidated into our financial statements that are reasonably likely to materially affect our liquidity or the availability of capital resources.

### **Item 7A. Quantitative and Qualitative Disclosures About Market Risk**

Market risk represents the risk of loss that may impact our financial position, operating results or cash flows due to changes in the U.S. interest rates. The primary objective of our investment activities is to preserve cash until it is required to fund operations. To minimize risk, we maintain our portfolio of cash and cash equivalents in operating bank accounts and money market funds. Since our investments are short-term in duration, we believe that we are not subject to any material market risk exposure. We do not have any foreign currency or other derivative financial instruments. On February 14, 2006 we issued \$10,000 of Convertible Debentures bearing interest at 7%.

### **Item 8. Financial Statements and Supplementary Data**

The financial statements required by this item are attached to this Annual Report on Form 10-K beginning on Page F-1.

### **Item 9. Changes In and Disagreements With Accountants on Accounting and Financial Disclosure**

None.

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**Item 9A. Controls and Procedures**

As of the end of the period covered by this Annual Report on Form 10-K, we carried out an evaluation, under the supervision and with the participation of our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures pursuant to Exchange Act Rules 13a-15(e) and 15d-15(e). Based on that evaluation, the Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective to ensure that information we are required to disclose in reports that we file or submit under the Exchange Act are recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. There has been no change in our internal controls over financial reporting that occurred during our fourth fiscal quarter of 2005 that has materially affected, or is reasonably likely to materially affect, our internal controls over financial reporting.

**Item 9B. Other Information**

None.

**PART III**

**Item 10. *Directors and Executive Officers of the Registrant***

The information required by this Item will be contained in our definitive Proxy Statement to be filed with the SEC in connection with our 2006 Annual Meeting of Stockholders to be held on May 25, 2006 (the "2006 Proxy Statement") under the captions "Election of Directors," "Board of Directors Meetings and Committees of the Board," "Executive Officers" and "Section 16(a) Beneficial Ownership Reporting Compliance" and is incorporated herein by reference.

We have adopted a Code of Ethics that applies to all our directors, officers and employees. The Code of Ethics is publicly available on our website at [www.pro-pharmaceuticals.com](http://www.pro-pharmaceuticals.com). Amendments to the Code of Ethics and any grant of a waiver from a provision of the Code of Ethics requiring disclosure under applicable SEC and American Stock Exchange rules will be disclosed on our website.

**Item 11. *Executive Compensation***

The information required by this Item is incorporated by reference from the information under the caption "Executive Compensation" contained in our 2006 Proxy Statement.

**Item 12. *Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters***

The information required by this item is incorporated by reference from the information under the caption "Ownership of Pro-Pharmaceuticals, Inc. Common Stock" contained in our 2006 Proxy Statement.

**Item 13. *Certain Relationships and Related Transactions***

The information required by this item is incorporated by reference from the information under the caption "Certain Relationships and Related Transactions" contained in our 2006 Proxy Statement.

**Item 14. *Principal Accountant Fees and Services***

The information required by this item is incorporated by reference from the information under the captions "Audit Fees," "Audit-Related Fees," "Tax Fees," "All Other Fees" and "Pre-Approval Policies and Procedures" contained in our 2005 Proxy Statement.

**PART IV****Item 15. Exhibits and Financial Statement Schedules**

## (a) 1. Consolidated Financial Statements

The Consolidated Financial Statements are filed as part of this report.

## 2. Consolidated Financial Statement Schedules

All schedules are omitted because of the absence of conditions under which they are required or because the required information is included in the Consolidated Financial Statements or notes thereto.

## 3. Exhibits

<u>Exhibit Number</u>	<u>Description of Document</u>	<u>Note Reference</u>
3.1	Articles of Incorporation of the Registrant, dated January 23, 2001	1
3.2	Amended and Restated By-laws of the Registrant	2
3.3	Certificate of Amendment to Articles of Incorporation of the Registrant, as filed with the Nevada Secretary of State on May 28, 2004	11
10.1	Assignment/Assumption Agreement, dated April 23, 2001, by and between Developed Technology Resource, Inc. and DTR-Med Pharma Corp.	1
10.2	Stock Exchange Agreement, dated April 25, 2001, by and among DTR-Med Pharma Corp., Developed Technology Resource, Inc., Pro-Pharmaceuticals, Inc. and the Shareholders (as defined therein)	1
10.3	Pro-Pharmaceuticals, Inc. 2001 Stock Incentive Plan	2
10.5	Consulting Agreement, dated as of January 16, 2003, by and between Pro-Pharmaceuticals, Inc. and David H. Smith	4
10.6	Employment Agreement, dated effective as of April 1, 2003, by and between Pro-Pharmaceuticals, Inc. and David A. Christopher (Agreement Terminated)	5
10.7	Securities Purchase Agreement, dated October 2, 2003, by and among Pro-Pharmaceuticals, Inc. and the Purchasers named therein	6
10.8	Registration Rights Agreement, dated October 2, 2003, by and among Pro-Pharmaceuticals, Inc. and the Purchasers named therein	6
10.9	Form of Common Stock Purchase Warrant issued to Rodman & Renshaw, Inc.	6
10.10	Form of Common Stock Purchase Warrant issued to the Purchasers under the Securities Purchase Agreement identified as Exhibit 10.7	6
10.11	Pro-Pharmaceuticals, Inc. 2003 Non-employee Director Stock Incentive Plan	7
10.12	Consulting Agreement, dated as of November 12, 2003, by and among Pro-Pharmaceuticals, Inc., The Harney Group and Charles F. Harney	8
10.13	Employment Agreement, dated effective as of January 2, 2004, by and between Pro-Pharmaceuticals, Inc. and David Platt	8
10.14	Securities Purchase Agreement, dated April 7, 2004, by and among Pro-Pharmaceuticals, Inc. and the Purchasers named therein	9
10.15	Registration Rights Agreement, dated April 7, 2004, by and among Pro-Pharmaceuticals, Inc. and the Purchasers named therein	9

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<u>Exhibit Number</u>	<u>Description of Document</u>	<u>Note Reference</u>
10.16	Form of Common Stock Purchase Warrant issuable pursuant to the Securities Purchase Agreement identified as Exhibit 10.14 and to the placement agent	9
10.17	Securities Purchase Agreement, dated August 12, 2004, by and among Pro-Pharmaceuticals, Inc. and the Purchasers named therein	10
10.18	Registration Rights Agreement, dated August 12, 2004, by and among Pro-Pharmaceuticals, Inc. and the Purchasers named therein	10
10.19	Form of Common Stock Purchase Warrant issuable pursuant to the Securities Purchase Agreement identified as Exhibit 10.17 and to the placement agent	10
10.20	Form of Incentive Stock Option Agreement (under the 2001 Stock Incentive Plan)	12
10.21	Form of Non-Qualified Stock Option Agreement (under the 2001 Stock Incentive Plan)	12
10.22	Form of Non-Qualified Stock Stock Option Agreement (under the 2003 Non-Employee Director Stock Incentive Plan)	12
10.23	Option Agreement, dated November 11, 2004, between David Platt and Pro-Pharmaceuticals, Inc.	12
10.24	Employment Agreement, dated February 9, 2005, between Carl L. Lueders and Pro-Pharmaceuticals, Inc.	13
10.25	7% Convertible Debenture dated February 14, 2006, Due February 14, 2008.	14
10.26	Securities Purchase Agreement, dated February 14, 2006, by and among Pro-Pharmaceuticals, Inc. and the Purchasers named therein	14
10.27	Registration Rights Agreement, dated February 14, 2006, by and among Pro-Pharmaceuticals, Inc. and the Purchasers named therein	14
10.28	Common Stock Purchase Warrant Agreement, dated February 14, 2006.	14
21.1	Subsidiaries of the Registrant	8
23.1*	Consent of Deloitte & Touche LLP, an independent registered public accounting firm	
31.1*	Certification Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934	
31.2*	Certification Pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934	
32.1**	Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	
32.2**	Certification Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	

\* Filed herewith.

\*\* Furnished herewith and not "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended.

1 Incorporated by reference to the Registrant's Registration Statement on Form 10-SB, as filed with the Commission on June 13, 2001.

2 Incorporated by reference to the Registrant's Quarterly Report on Form 10-QSB for the period ended September 30, 2001, as filed with the Commission on November 14, 2001.

3 Incorporated by reference to the Registrant's Current Report on Form 8-K as filed with the Commission on March 8, 2002.

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- 4 Incorporated by reference to the Registrant's Annual Report on Form 10-KSB for the fiscal year ended December 31, 2002, as filed with the Commission on March 31, 2003.
- 5 Incorporated by reference to the Registrant's Quarterly Report on Form 10-QSB for the period ended June 30, 2003, as filed with the Commission on August 14, 2003.
- 6 Incorporated by reference to the Registrant's Current Report on Form 8-K/A as filed with the Commission on October 10, 2003 for the period October 2, 2003.
- 7 Incorporated by reference to the Registrant's Registration Statement on Form S-8, as filed with the Commission on October 22, 2003.
- 8 Incorporated by reference to the Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2003, as filed with the Commission on March 30, 2004.
- 9 Incorporated by reference to the Registrant's Current Report on Form 8-K as filed with the Commission on April 9, 2004.
- 10 Incorporated by reference to the Registrant's Current Report on Form 8-K as filed with the Commission on August 16, 2004.
- 11 Incorporated by reference to the Registrant's Quarterly Report on Form 10-Q for the period ended June 30, 2004 as filed with the Commission on August 16, 2004.
- 12 Incorporated by reference to the Registrant's Quarterly Report on Form 10-Q for the period ended September 30, 2004 as filed with the Commission on November 19, 2004.
- 13 Incorporated by reference to the Registrant's Current Report on Form 8-K as filed with the Commission on February 11, 2005.
- 14 Incorporated by reference to the Registrant's Current Report on Form 8-K as filed with the Commission on February 15, 2006.

**SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on March 14, 2006.

PRO-PHARMACEUTICALS, INC.

By:     /s/    DAVID PLATT

Name: David Platt, Ph.D.  
Title: Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/    DAVID PLATT</u> David Platt, Ph.D.	President, Chief Executive Officer and Director	March 14, 2006
<u>/s/    CARL L. LUEDERS</u> Carl L. Lueders	Chief Financial Officer (Principal Financial and Accounting Officer)	March 14, 2006
<u>/s/    MILDRED S. CHRISTIAN</u> Mildred S. Christian, Ph.D.	Director	March 14, 2006
<u>/s/    DALE H. CONAWAY</u> Dale H. Conaway, D.V.M.	Director	March 14, 2006
<u>/s/    BURTON C. FIRTEL</u> Burton C. Firtel	Director	March 14, 2006
<u>/s/    STEVEN PRELACK</u> Steven Prelack	Director	March 14, 2006
<u>/s/    JERALD K. ROME</u> Jerald K. Rome	Director	March 14, 2006
<u>/s/    DAVID H. SMITH</u> David H. Smith	Director	March 14, 2006

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**Pro-Pharmaceuticals, Inc.**  
**(A Development Stage Company)**

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**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

To the Board of Directors and Stockholders of Pro-Pharmaceuticals, Inc., Newton, Massachusetts

We have audited the accompanying consolidated balance sheets of Pro-Pharmaceuticals, Inc. and subsidiary (a development stage company) (the "Company") as of December 31, 2005 and 2004, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2005, and for the period from inception (July 10, 2000) to December 31, 2005. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2005 and 2004, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2005, and for the period from inception (July 10, 2000) to December 31, 2005 in conformity with accounting principles generally accepted in the United States of America.

/s/ Deloitte & Touche LLP

Boston, Massachusetts

March 14, 2006

[Table of Contents](#)**PRO-PHARMACEUTICALS, INC.**  
**(A Development-Stage Company)****CONSOLIDATED BALANCE SHEETS**  
DECEMBER 31, 2005 AND 2004 (dollars in thousands)

	<u>2005</u>	<u>2004</u>
<b>ASSETS</b>		
<b>CURRENT ASSETS:</b>		
Cash and cash equivalents	\$ 4,466	\$ 10,704
Prepaid expenses and other current assets	228	120
<b>Total current assets</b>	<b>4,694</b>	<b>10,824</b>
<b>PROPERTY AND EQUIPMENT—NET</b>	<b>60</b>	<b>103</b>
<b>INTANGIBLE ASSETS—NET</b>	<b>209</b>	<b>156</b>
<b>DEPOSITS AND OTHER ASSETS</b>	<b>—</b>	<b>27</b>
<b>TOTAL ASSETS</b>	<b>\$ 4,963</b>	<b>\$ 11,110</b>
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
<b>CURRENT LIABILITIES:</b>		
Accounts payable	\$ 295	\$ 206
Other accrued expenses	1,085	799
<b>Total current liabilities</b>	<b>\$ 1,380</b>	<b>\$ 1,005</b>
<b>COMMITMENTS AND CONTINGENCIES (Note 9)</b>		
<b>STOCKHOLDERS' EQUITY:</b>		
Common stock, \$0.001 par value; 100,000,000 shares authorized; 27,315,411 and 27,315,411 shares of common stock issued and outstanding at December 31, 2005 and 2004, respectively; Undesignated shares, \$.01 par value; 10,000,000 and 5,000,000 shares authorized at December 31, 2005 and 2004, respectively	27	27
Additional paid-in capital	29,986	29,965
Deferred compensation	—	(1)
Deficit accumulated during the development stage	(26,430)	(19,886)
<b>Total stockholders' equity</b>	<b>3,583</b>	<b>10,105</b>
<b>TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY</b>	<b>\$ 4,963</b>	<b>\$ 11,110</b>

See notes to consolidated financial statements.

**PRO-PHARMACEUTICALS, INC.**  
**(A Development-Stage Company)****CONSOLIDATED STATEMENTS OF OPERATIONS**  
**YEARS ENDED DECEMBER 31, 2005, 2004 AND 2003, AND CUMULATIVE PERIOD**  
**FROM INCEPTION (JULY 10, 2000) TO DECEMBER 31, 2005 (dollars in thousands)**

	Years Ended December 31,			Cumulative Period from Inception (July 10, 2000) to December 31, 2005
	2005	2004	2003	
<b>OPERATING EXPENSES:</b>				
Research and development	\$ 3,040	\$ 3,042	\$ 1,950	\$ 10,509
General and administrative	3,615	4,262	2,988	14,024
Total operating expenses	(6,655)	(7,304)	(4,938)	(24,533)
INTEREST AND OTHER INCOME	111	124	69	354
<b>INTEREST AND OTHER EXPENSES:</b>				
Amortization of debt discount on convertible notes	—	—	—	1,258
Debt conversion expense	—	—	—	503
Interest expense on convertible notes	—	—	—	486
Other Interest Expense	—	—	4	4
Total interest and other expenses	—	—	4	(2,251)
NET LOSS	\$ (6,544)	\$ (7,180)	\$ (4,873)	\$ (26,430)
NET LOSS PER SHARE—BASIC AND DILUTED	\$ (0.24)	\$ (0.28)	\$ (0.23)	
WEIGHTED AVERAGE COMMON SHARES OUTSTANDING—BASIC AND DILUTED	27,315,411	25,750,789	21,360,572	

See notes to consolidated financial statements.

**PRO-PHARMACEUTICALS, INC.**  
**(A Development-Stage Company)**

**CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY**  
**YEARS ENDED DECEMBER 31, 2005, 2004 AND 2003, AND CUMULATIVE PERIOD**  
**FROM INCEPTION (JULY 10, 2000) TO DECEMBER 31, 2005 (dollars in thousands)**

	Common Stock		Additional Paid-in Capital	Deferred Compensation	Deficit Accumulated During the Development Stage	Total Stockholders' Equity
	Number of Shares	\$0.001 Par Value				
Issuance of founders shares	12,354,670	\$ 12	\$ (3)	\$ —	\$ —	\$ 9
Beneficial conversion feature and rights to common stock embedded in convertible note	—	—	222	—	—	222
Net loss	—	—	—	—	(185)	(185)
<b>BALANCE, DECEMBER 31, 2000</b>	<b>12,354,670</b>	<b>12</b>	<b>219</b>	<b>—</b>	<b>(185)</b>	<b>46</b>
Issuance of common stock and beneficial conversion feature related to convertible note	660,321	1	1,035	—	—	1,036
Issuance of common stock in connection with reverse merger of Pro- Pharmaceuticals-NV	1,221,890	1	106	—	—	107
Conversion of notes payable and accrued interest to common stock	598,229	1	1,125	—	—	1,126
Issuance of warrants to induce conversion of notes payable	—	—	503	—	—	503
Issuance of common stock and warrants (net of issuance costs of \$17)	689,300	1	2,220	—	—	2,221
Deferred compensation relating to issuance of stock options	—	—	239	(239)	—	—
Amortization of deferred compensation	—	—	—	147	—	147
Net loss	—	—	—	—	(3,970)	(3,970)
<b>BALANCE, DECEMBER 31, 2001</b>	<b>15,524,410</b>	<b>16</b>	<b>5,447</b>	<b>(92)</b>	<b>(4,155)</b>	<b>1,216</b>
Issuance of common stock (net of issuance costs of \$49)	185,999	*	602	—	—	602
Issuance of common stock related to 2002 private placement (net of issuance costs of \$212)	3,223,360	3	2,858	—	—	2,861
Conversion of notes payable and accrued interest to common stock	100,878	*	275	—	—	275
Stock compensation expense related to issuance of options to consultant	—	—	41	—	—	41
Issuance of warrants to purchase common stock in consideration for placement of convertible notes payable	—	—	236	—	—	236
Deferred compensation relating to issuance of stock options	—	—	11	(11)	—	—
Amortization of deferred compensation	—	—	—	48	—	48
Stock compensation expense related to fair market revaluation	—	—	16	—	—	16
Net loss	—	—	—	—	(3,678)	(3,678)
<b>BALANCE, DECEMBER 31, 2002</b>	<b>19,034,697</b>	<b>19</b>	<b>9,486</b>	<b>(55)</b>	<b>(7,833)</b>	<b>1,617</b>

(Continued)

**PRO-PHARMACEUTICALS, INC.**  
**(A Development-Stage Company)**

**CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY**  
**YEARS ENDED DECEMBER 31, 2005, 2004 AND 2003, AND CUMULATIVE PERIOD**  
**FROM INCEPTION (JULY 10, 2000) TO DECEMBER 31, 2005 (dollars in thousands)**

	Common Stock		Additional Paid-in Capital	Deferred Compensation	Deficit Accumulated During the Development Stage	Total Stockholders' Equity
	Number of Shares	\$0.001 Par Value				
BALANCE, DECEMBER 31, 2002	19,034,647	19	9,486	(55)	(7,833)	1,617
Issuance of common stock to investors in 2002 Private Placement (net of issuance costs of \$18)	1,088,000	1	1,069	—	—	1,070
Issuance of common stock to consultants for services related to 2002 Private Placement	12,250	*	12	—	—	12
Receipt of subscription receivable	—	—	150	—	—	150
Conversion of accrued expenses to common stock and options	201,704	*	302	—	—	302
Issuance of common stock to investors in 2003 private placements (net of issuance costs of \$688)	3,719,070	4	7,029	—	—	7,033
Fair value of common stock warrants issued to investors in 2003 private placements	—	—	1,242	—	—	1,242
Fair value of common stock warrants issued to placement agents in October, 2003 private placements	—	—	452	—	—	452
Stock compensation expense related to issuance of common stock and options	7,000	*	149	—	—	149
Issuance of common stock options in consideration for investor relations services	—	—	29	—	—	29
Stock compensation expense related to accelerated option vesting	—	—	40	—	—	40
Cashless exercise of employee stock options	16,629	*	74	—	—	74
Deferred compensation relating to issuance of stock options	—	—	205	(205)	—	—
Amortization of deferred compensation	—	—	—	327	—	327
Deferred compensation expense related to fair market revaluation	—	—	137	(137)	—	—
Net loss	—	—	—	—	(4,873)	(4,873)
BALANCE, DECEMBER 31, 2003	24,079,300	\$ 24	\$ 20,376	\$ (70)	\$ (12,706)	\$ 7,624

(Continued)

\* Amounts less than \$500

See notes to consolidated financial statements.

**PRO-PHARMACEUTICALS, INC.**  
**(A Development-Stage Company)**

**CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY**  
**YEARS ENDED DECEMBER 31, 2005, 2004 AND 2003, AND CUMULATIVE PERIOD**  
**FROM INCEPTION (JULY 10, 2000) TO DECEMBER 31, 2005 (dollars in thousands)**

	Common Stock		Additional Paid-in Capital	Deferred Compensation	Deficit Accumulated During the Development Stage	Total Stockholders' Equity
	Number of Shares	\$0.001 Par Value				
BALANCE, DECEMBER 31, 2003	24,079,300	\$ 24	\$ 20,376	\$ (70)	\$ (12,706)	\$ 7,624
Issuance of common stock to investors in April, 2004 private placement (net of issuance costs of \$466)	1,236,111	1	2,664	—	—	2,665
Fair value of common stock warrants issued to investors on April, 2004 private placement	—	—	1,164	—	—	1,164
Fair value of common stock warrants issued to placement agent in April, 2004 private placement	—	—	154	—	—	154
Issuance of common stock to investors in August, 2004 private placement (net of issuance costs of \$485)	2,000,000	2	2,791	—	—	2,793
Fair value of common stock warrants issued to investors in August, 2004 private placement	—	—	2,483	—	—	2,483
Fair value of common stock warrants issued to placement agent in August, 2004 private placement	—	—	239	—	—	239
Issuance of common stock options in consideration for investor relations services	—	—	90	—	—	90
Amortization of deferred compensation	—	—	—	73	—	73
Deferred compensation expense related to fair market revaluation	—	—	4	(4)	—	—
Net loss	—	—	—	—	(7,180)	(7,180)
BALANCE, DECEMBER 31, 2004	27,315,411	\$ 27	\$ 29,965	\$ (1)	\$ (19,886)	\$ 10,105
Issuance of common stock options in consideration for investor relations and other services	—	—	21	—	—	21
Amortization of deferred compensation	—	—	—	1	—	1
Net loss	—	—	—	—	(6,544)	(6,544)
BALANCE, DECEMBER 31, 2005	27,315,411	\$ 27	\$ 29,986	\$ —	\$ (26,430)	\$ 3,583

(Concluded)

See notes to consolidated financial statements.

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**PRO-PHARMACEUTICALS, INC.**  
**(A Development-Stage Company)**

**CONSOLIDATED STATEMENTS OF CASH FLOWS**  
**YEARS ENDED DECEMBER 31, 2005, 2004 AND 2003, AND CUMULATIVE PERIOD**  
**FROM INCEPTION (JULY 10, 2000) TO DECEMBER 31, 2005 (dollars in thousands)**

	Years Ended December 31,			Cumulative Period from Inception (July 10, 2000) to December 31, 2005
	2005	2004	2003	
<b>CASH FLOWS FROM OPERATING ACTIVITIES:</b>				
Net loss	\$ (6,544)	\$ (7,180)	\$ (4,873)	\$ (26,430)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation and amortization	81	81	89	307
Stock-based compensation expense	23	162	619	1,057
Amortization of deferred extension costs through interest expense	—	—	—	167
Settlement of accrued interest through issuance of common stock	—	—	—	10
Amortization of debt discount on convertible notes	—	—	—	1,258
Write-off of intangible assets	20	9	—	136
Debt conversion expense	—	—	—	503
Interest expense related to issuance of warrants to purchase common stock	—	—	—	236
Changes in current assets and liabilities:				
Prepaid expenses and other current assets	(81)	(32)	(16)	(198)
Deposits and other assets	—	—	—	(27)
Accounts payable and accrued expenses	374	627	29	1,498
Net cash used in operating activities	(6,127)	(6,333)	(4,152)	(21,483)
<b>CASH FLOWS FROM INVESTING ACTIVITIES:</b>				
Purchases of property and equipment	(21)	(23)	(39)	(316)
Increase in patents costs and other assets	(90)	(46)	(66)	(288)
Net cash used in investing activities	(111)	(69)	(105)	(604)
<b>CASH FLOWS FROM FINANCING ACTIVITIES:</b>				
Net proceeds from issuance of common stock and warrants	—	9,498	9,944	25,309
Net proceeds from issuance of convertible notes payable	—	—	—	1,321
Repayment of convertible notes payable	—	—	—	(86)
Proceeds from shareholder advances	—	—	—	9
Net cash provided by financing activities	—	9,498	9,944	26,553
NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	(6,238)	3,096	5,687	4,466
CASH AND CASH EQUIVALENTS, BEGINNING OF PERIOD	10,704	7,608	1,921	—
CASH AND CASH EQUIVALENTS, END OF PERIOD	\$ 4,466	\$ 10,704	\$ 7,608	\$ 4,466
SUPPLEMENTAL DISCLOSURE – Cash paid for interest	\$ —	\$ —	\$ —	\$ 19
<b>NONCASH FINANCING ACTIVITIES</b>				
Issuance of warrants in connection with equity offerings	—	4,040	1,503	6,645
Conversion of accrued expenses into common stock	—	—	303	303
Cashless exercise of employee stock options	—	—	74	74
Conversion of convertible notes and accrued interest into common stock	—	—	—	1,220
Conversion of extension costs related to convertible notes into common stock	—	—	—	171
Issuance of warrants to induce conversion of notes payable	—	—	—	503
Issuance of stock to acquire Pro-Pharmaceuticals-NV	—	—	—	107

See notes to consolidated financial statements.

**PRO-PHARMACEUTICALS, INC.**  
**(A DEVELOPMENT-STAGE COMPANY)**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (dollar amounts in thousands)**

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**1. NATURE OF BUSINESS AND BASIS OF PRESENTATION**

Pro-Pharmaceuticals, Inc. (the “Company”) is a development stage life sciences company established in July 2000. The Company is developing technologies that are intended to reduce toxicity and improve the efficacy of chemotherapy drugs by combining the drugs with proprietary carbohydrate compounds. The carbohydrate-based drug delivery compounds may also have application for drugs to treat other diseases and chronic health conditions.

The Company is devoting substantially all of its efforts toward product research and development, and raising capital. Its first product candidate began a Phase I clinical trial in February 2003. Patient dosing in this trial was completed in March 2005. This same product candidate began a concurrent Phase II clinical trial in January 2004. Patient dosing in this trial commenced in May of 2005

As shown in the consolidated financial statements, the Company incurred net losses of \$26,430 for the cumulative period from inception (July 10, 2000) through December 31, 2005. The Company expects to incur additional losses and use additional cash in its operations in the near future. Through December 31, 2005, the Company had raised \$26,630 in capital through (i) the issuance of convertible notes; (ii) the sale of common stock through a public offering; and (iii) the sale of common stock and warrants through private placements. From inception (July 10, 2000) through December 31, 2005, the Company used cash of \$21,483 in its operations. At December 31, 2005, the Company had \$4,466 of cash and cash equivalents available to fund future operations, which when combined with approximately \$9.3 million net of transaction costs raised through the sale of convertible debentures issued on February 14, 2006 (see Note 11), management believes is sufficient cash to fund its operations through at least June 2007.

The Company is subject to a number of risks similar to those of other development-stage companies, including dependence on key individuals, uncertainty of product development and generation of revenues, dependence on outside sources of capital, risks associated with clinical trials of products, dependence on third-party collaborators for research operations, need for regulatory approval of products, risks associated with protection of intellectual property, and competition with larger, better-capitalized companies. Successful completion of the Company’s development program and, ultimately, the attainment of profitable operations is dependent upon future events, including obtaining adequate financing to fulfill its development activities and achieving a level of revenues adequate to support the Company’s cost structure. There are no assurances, however, that the Company will be able to obtain additional financing on favorable terms, or at all, or successfully market its products.

**2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES**

The accompanying consolidated financial statements reflect the application of certain accounting policies, as described in this note and elsewhere in the accompanying notes to financial statements.

*Basis of Consolidation* – The consolidated financial statements include the accounts of the Company and Pro-Pharmaceuticals Securities Corp., its wholly owned subsidiary, which was incorporated in Delaware on December 23, 2003. All significant intercompany transactions have been eliminated.

*Use of Estimates* – The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue, expenses and disclosure of contingent assets

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and liabilities. Management's estimates are based primarily on historical experience and on various other assumptions that are believed to be reasonable under the circumstances. Actual results could differ from those estimates.

*Cash and Cash Equivalents* – The Company considers all highly liquid investments with original maturities of 90 days or less at the time of acquisition to be cash equivalents.

*Property and Equipment* – Property and equipment, including leasehold improvements, are stated at cost, net of accumulated depreciation, and are depreciated using the straight-line method over the lesser of the estimated useful lives of the assets or the related lease term.

The estimated useful lives of property and equipment are as follows:

<u>Asset Classification</u>	<u>Estimated Useful Life</u>
Computers and office equipment	Three years
Furniture and fixtures	Five years
Leasehold improvements	Life of lease

*Intangible Assets* – Intangible assets include patent costs, consisting primarily of related legal fees, which are capitalized as incurred and amortized over an estimated useful life of five years from issuance. Amortization expense in 2005, 2004 and 2003 was \$17, \$17 and \$17 respectively and accumulated amortization at December 31, 2005 totaled \$50.

*Deposits and Other Assets* – Deposits and other assets consist principally of lease deposits on the Company's leased executive office space.

*Long-Lived Assets* – In accordance with Statement of Financial Accounting Standards ("SFAS") No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets", the Company reviews all long-lived assets for impairment whenever events or circumstances indicate the carrying amount of such assets may not be recoverable. Recoverability of assets to be held or used is measured by comparison of the carrying value of the asset to the future undiscounted net cash flows expected to be generated by the asset. If such asset is considered to be impaired, the impairment recognized is measured by the amount by which the carrying value of the asset exceeds the discounted future cash flows expected to be generated by the asset.

In the fourth quarter of 2005 the Company wrote off \$20 of capitalized patent costs when it was determined that the underlying intellectual property would have no future benefit to the Company. In 2004 the Company wrote off \$9 of capitalized patent costs when it was determined that the underlying intellectual property would have no future benefit to the Company. In 2003 the Company recorded no adjustment to the carrying value of the long-lived assets.

*Research and Development Expenses* – Costs associated with research and development are expensed as incurred. Research and development expenses include, among other costs, salaries and other personnel-related costs, and costs incurred by outside laboratories and other accredited facilities in connection with clinical trials and preclinical studies.

*Income Taxes* – The Company accounts for income taxes in accordance with SFAS No. 109, "Accounting for Income Taxes". This statement requires an asset and liability approach to accounting for income taxes based upon the future expected values of the related assets and liabilities. Deferred income tax assets and liabilities are determined based on the differences between the financial reporting and tax bases of assets and liabilities and for tax loss and credit carryforwards, and are measured using the expected tax rates estimated to be in effect when such basis differences reverse. Valuation allowances are established, if necessary, to reduce the deferred tax asset to the amount that will, more likely than not, be realized.

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*Loss per Share* – Basic and diluted loss per share is presented in conformity with SFAS No. 128, “Earnings Per Share”. Basic loss per share is calculated using the weighted-average number of common shares outstanding during the year. Diluted loss per share is calculated using the weighted-average number of common shares and common share equivalents resulting from outstanding options and warrants, except where such items would be anti-dilutive.

The loss used to calculate basic and diluted loss per share for the years ended December 31, 2005, 2004 and 2003 was equal to the reported net loss for each period.

A reconciliation between the shares used for computation of basic and diluted income per share is as follows:

	2005	2004	2003
Shares for basic computation	27,315,411	25,750,789	21,360,572
Effect of dilutive stock options and warrants	—	—	—
Shares for dilutive computation	27,315,411	25,750,789	21,360,572

Anti-dilutive shares were not included in the per-share calculations for the years ended December 31, 2005, 2004 and 2003 due to the reported net losses for those years. Anti-dilutive shares which could exist pursuant to the exercise of outstanding stock options and warrants and conversion of convertible debt at December 31, 2005, 2004 and 2003 totaled approximately 6,397,851, 7,377,952 and 4,434,890 respectively.

*Comprehensive Income (Loss)* – Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. The Company does not have any items of comprehensive income (loss) other than net losses as reported.

*Fair Value of Financial Instruments* – SFAS No. 107, “Disclosures About Fair Value of Financial Instruments,” requires disclosure of the fair value of certain financial instruments. The Company’s financial instruments consist of cash equivalents, accounts payable and accrued expenses. The estimated fair value of these financial instruments approximates their carrying value due to their short-term nature.

*Concentration of Credit Risk* – The Company has no significant concentrations of credit risk, such as foreign exchange contracts or other hedging arrangements. Financial instruments that subject the Company to credit risk consist of cash and cash equivalents. The Company maintains cash equivalents with well-capitalized financial institutions.

*Segment Information* – SFAS No. 131, “Disclosures about Segments of an Enterprise and Related Information”, requires companies to report selected information about operating segments, as well as enterprise-wide disclosures about products, services, geographic areas and major customers. Operating segments are determined based on the way management organizes its business for making operating decisions and assessing performance. The Company has concluded that it operates in one operating segment.

*Stock-Based Compensation* – At December 31, 2005, the Company has two equity incentive plans, which are described more fully in Note 8. The Company accounts for stock-based compensation to employees and non-employee directors under the intrinsic method in accordance with Accounting Principles Board (“APB”) Opinion No. 25, “Accounting for Stock Issued to Employees,” and the related interpretations. Under APB No. 25, no compensation expense is recognized for stock options and restricted stock awards granted at fair market value and with fixed terms.

Stock or other equity-based compensation granted to non-employees is accounted for under the fair value method in accordance with SFAS No. 123, “Accounting for Stock-Based Compensation”, and the Emerging

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Issues Task Force (“EITF”) Abstract No. 96-18, “Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services,” and the related interpretations. Under this method, compensation is recorded at the fair value of the consideration received or the fair value of the equity instrument until the final measurement date, which is the earlier of performance completion or vesting. Compensation related to stock appreciation rights and other variable stock option or award plans are remeasured at the end of each reporting period. Fluctuations in the quoted market price of the Company’s stock covered by unvested equity instruments are reflected as an adjustment to deferred compensation and compensation expense over the periods the related service is performed. Stock-based compensation expense totaled \$23, \$162 and \$619 in 2005, 2004 and 2003 respectively.

The fair value of the equity instruments granted to non-employees, including options and warrants, is determined using the Black-Scholes option-pricing model. Key assumptions used to apply this option-pricing model are as follows:

	2005	2004	2003	Cumulative Period from Inception (July 10, 2000) to December 31, 2005
Risk-free interest rate	3.43% - 4.52%	2.00% - 3.28%	1.51% - 2.45%	1.51% - 4.52%
Expected life of the options and warrants	3 years	3 years	3 years	3 years
Expected volatility of the underlying stock	75%	95%	95%	95%
Expected dividend rate	None	None	None	None

Had the Company used the fair-value method to measure all stock-based compensation awarded to employees and non-employee directors, the Company’s net loss and basic and diluted loss per share would have been as follows at December 31:

	2005	2004	2003	Cumulative Period from Inception (July 10, 2000) to December 31, 2005
Net loss—as reported	\$(6,544)	\$(7,180)	\$(4,873)	\$ (26,430)
Deduct stock-based compensation determined under the fair-value method	(287)	(749)	(2,824)	(4,214)
Net loss—pro forma	<u>\$(6,831)</u>	<u>\$(7,929)</u>	<u>\$(7,697)</u>	<u>\$ (30,644)</u>
Basic and diluted loss per share:				
As reported	\$ (0.24)	\$ (0.28)	\$ (0.23)	
Pro forma	<u>\$ (0.25)</u>	<u>\$ (0.31)</u>	<u>\$ (0.36)</u>	

The 2005 stock-based compensation amount of \$287 includes \$59 related to 34,000 options for Board of Directors service which were earned in 2005 but not granted.

In December 2004, the Financial Accounting Standards Board issued SFAS No. 123(R), “Share-Based Payment” (SFAS 123R). This Statement is a revision of SFAS No. 123, “Accounting for Stock-Based Compensation,” and supersedes Accounting Principles Board Opinion No. 25, “Accounting for Stock Issued to Employees,” and its related implementation guidance. SFAS 123R requires a company to measure the grant date fair value of equity awards given to employees in exchange for services and recognize that cost over the period that such services are performed. The Company adopted SFAS 123R on January 1, 2006,

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using the modified-prospective transition method. Adoption of SFAS 123R will materially increase the Company's stock compensation expense, net loss and net loss per share; it will not, however, have an impact on the Company's financial position. For fiscal year 2006, total stock-based compensation expense, including amounts from stock options using the fair value provisions of SFAS 123R, is estimated to be approximately \$155. In order to develop the fiscal 2006 stock-based compensation expense estimate, the Company utilized assumptions, including, among other items, expected life and volatility, which reflect assumptions used in 2005. Total unrecognized stock-based compensation expense related to unvested stock options and unvested restricted stock awards, expected to be recognized over a weighted average period of 2 years, amounted to \$159 at December 31, 2005. The amounts reflected above represent the unamortized value of existing option grants at December 31, 2005. While it is likely that stock options will be granted in 2006, no estimate of 2006 grants has been included in the 2006 estimate of stock based compensation expense.

### 3. PROPERTY AND EQUIPMENT

Property and equipment consists of the following at December 31:

	2005	2004
Leasehold improvements	\$ 104	\$ 104
Computer and office equipment	132	110
Furniture and fixtures	81	81
Total	317	295
Less accumulated depreciation	(257)	(192)
Property and equipment—net	\$ 60	\$ 103

### 4. OTHER ACCRUED EXPENSES

Other accrued expenses consist of the following at December 31:

	2005	2004
Legal and accounting fees	\$ 188	\$ 250
Scientific and clinical fees	578	374
Accrued payroll	296	116
Other	23	59
Total	\$ 1,085	\$ 799

### 5. RELATED PARTY TRANSACTIONS

The Company has entered into various consulting agreements, each terminable on thirty days notice, with certain related parties as follows: (i) a corporation controlled by a person who is a stockholder, and former director and officer, of the Company for financing and business development services (subsequently terminated when such person became an employee of the Company in 2002), (ii) a corporation controlled by a person who is a stockholder, and former officer, of the Company for research and development services, including reimbursable expenses, (iii) an individual who is a stockholder of the Company for management and consultant services, and (iv) a corporation controlled by a person who is a stockholder and director of the Company for scientific advisory services. The total related party consulting expenses and related expenses paid to these corporations and individuals were \$153, \$178, and \$162 for 2005, 2004 and 2003 respectively.

In addition, the stockholder and director of the Company described under (iv) above agreed to receive compensation for certain 2002 scientific advisory services in the form of 25,354 shares of common stock

and 25,354 options at an exercise price of \$2.96 to purchase common stock of the Company. As of December 31, 2002, the Company recorded the deemed fair value of such compensation of approximately \$122 as an accrued liability. The common stock has been valued at \$76, based on the closing price of the publicly traded shares of common stock on the date of grant. The options were valued at \$46 using the Black-Scholes option-pricing model, based on a deemed fair value of the Company's common stock of \$3.00 per share. The accrued liability at December 31, 2002 was converted to equity in 2003 when the 25,354 shares of common stock and 25,354 options were issued to this individual.

## 6. CONVERTIBLE NOTES

During 2001 and 2000, the Company issued \$1,036 and \$285 of convertible notes, respectively. In August 2001, the Company offered warrants to holders of its outstanding convertible notes as an inducement to convert prior to the maturity of the notes. Holders representing \$1,126 of the outstanding principal and accrued interest chose to convert at a conversion price of \$2.00 per share and received 598,229 common shares and 562,801 warrants. The warrants expired unexercised in 2005. As described in Note 7, the Company valued the warrants at \$503 using the Black-Scholes option-pricing model, and recorded such value as a debt conversion 2001.

In May 2002, the Company extended the maturity date on the \$195 of convertible notes payable at December 31, 2001. In consideration for the extension, the holders received one-quarter of one share of the Company's common stock for each whole dollar amount of principal outstanding, or 48,750 shares of common stock. The Company deferred \$171 in costs associated with the extension, based on the fair value of the Company's common stock of \$3.50 at the time of the extension. These deferred convertible notes payable costs were amortized ratably over the twelve-month extended term of the notes, or expensed immediately upon conversion of the note prior to the extended maturity date.

In June 2002, \$80 in convertible notes payable and \$10 in related accrued interest was converted into 45,128 shares of common stock. In October 2002, the Company settled a convertible note payable of \$100 through a cash payment of \$86 and conversion of the remaining \$14 of principal into 7,000 shares of common stock pursuant to the original terms of the note. In addition, \$17 of related accrued interest was repaid in cash.

During 2002, \$167 of the deferred convertible notes payable extension costs was amortized to expense.

## 7. STOCKHOLDERS' EQUITY

*2001 Private Placement* – From May 25, 2001 through December 3, 2001, the Company sold a total of 689,300 shares of common stock for proceeds of \$2,221, net of \$17 of issuance costs through a private placement of securities (the "2001 Private Placement"). Each share sold in the 2001 Private Placement included a warrant to purchase common stock of the Company. These warrants are described below.

*Public Offering* – On December 13, 2001, the Company commenced a public offering of 1,428,572 shares of common stock, at a price to the public of \$3.50 per share. The Company concluded the offering on June 30, 2002. The Company sold 185,999 shares of common stock in this offering for proceeds of \$602, net of \$49 of issuance costs, all in 2002.

*2002 Private Placement* – In September 2002, the Company began a private placement (the "2002 Private Placement") of up to 10 million shares of common stock at \$1.00 per share, exempt from registration pursuant to Rule 506 of Regulation D under the Securities Act of 1933. As of December 31, 2002, the Company had sold 3,223,360 shares for proceeds of \$2,861, net of issuance costs of \$212 and stock subscription receivable of \$150, which related to shares purchased but for which payment had not been received as of December 31, 2002. This offering was closed on January 14, 2003, although subsequent to year end the Company sold an additional 1,088 shares for additional proceeds of \$1,071, net of \$18 of offering costs.

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The Company compensated a registered investment adviser with respect to shares purchased by its clients. As of December 31, 2002, the adviser was entitled to receive 173,500 shares of common stock. The Company also agreed to compensate a finder registered under applicable law, and such finder's agents, for identifying qualified investors. As of December 31, 2002, one of the finder's agents was entitled to receive 750 shares of common stock. On January 14, 2003, the Company closed the 2002 Private Placement, at which point the Company agreed to issue the adviser an additional 2,500 shares, and the finder and its other agent an aggregate of 9,750 additional shares and \$3 in cash in connection with the shares sold subsequent to December 31, 2002 and through the closing date.

Shares placed by such registered adviser, finder and finder's agent were accounted for as offering costs and valued at \$1.00 per share, consistent with the price paid for the shares placed in the offering. Such offering costs were netted against the proceeds of the 2002 Private Placement. Since none of the 174,250 shares had been issued as of December 31, 2002, the Company recorded the obligation to issue such shares as offering costs payable. The additional 12,250 shares issued in January 2003 were also valued at \$1.00 per share and included in the \$18 offering costs recorded at the closing.

During 2002, the Company also agreed to issue 2,100 shares of common stock to an employee for finding investors in connection with the 2002 Private Placement. None of the shares had been issued as of December 31, 2002. Accordingly, the Company recorded the obligation to general and administrative expenses in the statement of operations in the amount of \$6. On January 14, 2003, the Company closed the 2002 Private Placement, at which point the Company agreed to issue such employee an additional 7,000 shares in connection with shares sold subsequent to December 31, 2002 and through the closing date. The Company recorded an additional obligation of \$21 to general and administrative expenses in 2003 representing the fair value of the additional 7,000 shares.

*May 2003 Private Placement* – In May 2003, the Company began a private placement of up to 2.5 million shares of common stock at \$2.00 per share, exempt from registration pursuant to Rule 506 of Regulation D under the Securities Act of 1933. As of the closing on July 15, 2003, the Company had sold 2,399,500 shares of common stock for proceeds of \$4,394, net of issuance costs of \$405. The issuance costs include \$261 related to the fair value of 109,613 common stock warrants (exercisable at \$5.40 per share) issued to the finders in connection with the offering. These warrants are described below.

*October 2003 "PIPE" Transaction* – On October 2, 2003 the Company closed a private offering, structured as a so-called "PIPE" (Private Investment, Public Equity), exempt from registration under Section 4(2) of the Securities Act of 1933, in which it sold to institutional investors 1,314,571 of the 1,428,571 offered shares of common stock at \$3.50 per share and 657,293 common stock warrants (initially exercisable at \$5.29 per share and currently exercisable at \$4.99 per share) for proceeds of \$3,866, net of issuance costs of \$735. The issuance costs include \$191 related to the fair value of 65,729 common stock warrants (initially exercisable at \$6.86 per share and currently exercisable at \$6.24 per share) issued to the placement agent in connection with this offering. These warrants are described below.

*April 2004 "PIPE" Transaction* – On April 7, 2004, the Company closed a private equity offering, structured as a "PIPE" and exempt from registration under Section 4(2) of the Securities Act of 1933, in which it sold to certain institutional investors 1,236,111 shares of common stock and 618,056 common stock warrants (initially exercisable at \$5.30 per share and currently exercisable at \$5.07 per share) at \$3.60 per share for proceeds of approximately \$3,984, net of cash issuance costs of approximately \$466. The placement agent also received 61,806 common stock warrants (initially exercisable at \$5.30 per share and currently exercisable at \$5.07 per share) in connection with this offering. These warrants are described below.

*August 2004 "PIPE" Transaction* – On August 12, 2004, the Company closed a private offering, structured as a "PIPE" and exempt from registration under Section 4(2) of the Securities Act of 1933, in which it sold

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to certain institutional investors 2,000,000 shares of common stock in tandem with 2,000,000 common stock warrants (exercisable at \$4.20 per share) at \$3.00 per share for proceeds of approximately \$5,515, net of cash issuance costs of approximately \$485. The placement agent also received 100,000 common stock warrants (exercisable at \$4.20 per share) in connection with this offering. These warrants are described below.

*Common Stock Warrants* – The Company has issued common stock warrants in connection with the execution of certain equity and debt financings and consulting agreements. The fair value of common stock warrants is determined using the Black-Scholes option-pricing model. The key assumptions are described in Note 2.

The following table summarizes information with regard to outstanding warrants issued in connection with equity and debt financings as of December 31, 2005:

<u>Issued in Connection With</u>	<u>Number Issued</u>	<u>Exercise Price</u>	<u>Exercisable Date</u>	<u>Expiration Date</u>
Placement Agents	110,000	3.50	February 1, 2002	February 1, 2012
May 2003 Private Placement				
Placement Agents	109,613	5.40	July 15, 2003	July 15, 2006
October 2003 PIPE Transaction				
Investors	657,293	4.99	October 2, 2003	October 2, 2008
Placement Agent	65,729	6.24	October 2, 2003	October 2, 2006
April 2004 PIPE Transaction				
Investors	618,056	5.07	April 7, 2004	April 7, 2009
Placement Agent	61,806	5.07	April 7, 2004	April 7, 2007
August 2004 PIPE Transaction				
Investors	2,000,000	4.20	February 13, 2005	August 12, 2009
Placement Agent	100,000	4.20	February 13, 2005	August 12, 2009
Total	3,722,497			

None of the above warrants have been exercised as of December 31, 2005.

In connection with the 2001 Private Placement, the Company issued 339,200 and 350,100 warrants to purchase common stock at \$6.50 and \$5.00 per share, respectively. The Company, upon giving written notice, may accelerate the exercise of the warrants and effect an early termination thereof in the event of either of the following: (i) the Company files a new drug application (“NDA”) with the Food and Drug Administration or (ii) the market price exceeds \$11.00 and \$10.00 for warrants with exercise prices of \$6.50 and \$5.00, respectively on any 10 trading days within a period of 20 consecutive trading days, as defined. In the event of acceleration, the unexercised warrants automatically terminate without payment by the Company upon the thirtieth day following the written notice. The Company valued the warrants at \$886, based on a deemed fair market value of the Company’s common stock of \$2.28 per share. All of these warrants expired unexercised in 2005.

As described in Note 6, in August 2001, the Company offered warrants to holders of its outstanding convertible notes as an inducement to convert prior to the maturity of the notes. Holders representing \$1,126 of the outstanding principal and accrued interest chose to convert at a conversion price of \$2.00 per share and received 598,229 common shares and 562,801 warrants. These warrants have an exercise price of \$6.50 per share and are immediately exercisable. The Company may, upon giving written notice, accelerate the exercise of the warrant and effect an early termination thereof in the event of either of the following: (i) the Company files a new drug application (“NDA”) with the Food and Drug Administration, or (ii) the market price exceeds \$11.00 on any 10 trading days within a period of 20 consecutive trading days as defined. In the event of acceleration, the unexercised warrants automatically terminate without payment by the

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Company upon the thirtieth day following the written notice. The Company valued the warrants at \$503 based on a deemed fair market value of the Company's common stock of \$2.28 per share. The value of the warrants has been recorded as a debt conversion expense. All of these warrants expired unexercised in 2005.

In 2002, the Company issued 110,000 warrants to the agents in connection with the 2001 debt offering. The warrants are exercisable immediately at an exercise price of \$3.50 per share and have a 10 year life. The Company valued these warrants at \$236 based on a deemed fair value of the Company's common stock of \$3.50 per share and recorded such value as interest expense in the statement of operations for the year ended December 31, 2002.

In connection with the May 2003 Private Placement, the Company issued 109,613 warrants exercisable at \$5.40 per share to its placement agents. The Company valued the warrants at \$261 based on a fair market value of the Company's common stock of \$4.30 per share and recorded the warrant value as offering costs with a corresponding increase to additional paid-in capital.

In connection with the October 2003 PIPE transaction, the Company issued 657,293 warrants with an initial exercise price of \$5.29 per share to the investors and 65,729 warrants with an initial exercise price of \$6.86 per share to its placement agent. The exercise price of the warrants is subject to adjustment pursuant to anti-dilution and other provisions. The fair value of the warrants was determined based on a fair market value of the Company's common stock of \$5.29 per share. As the shares of common stock were issued at a discount to their fair market value at the closing of the October 2003 PIPE transaction, the Company used the relative fair value method to record the value of the warrants to the investors. Accordingly, \$1,242 of the proceeds has been attributed to such warrants and recorded as an increase to additional paid-in capital. In addition, the \$191 fair value of the warrants issued to the placement agent has been recorded as an increase to additional paid-in capital.

In connection with the April 2004 PIPE transaction, the Company issued 618,056 and 61,806 warrants with an initial exercise price of \$5.30 per share to the investors and to the placement agent, respectively. The exercise price of the warrants is subject to adjustment pursuant to anti-dilution and other provisions. The fair value of the warrants was determined based on a fair market value of the Company's common stock of \$4.41 per share. As the shares of common stock were issued at a discount to their fair market value at the closing of the April 2004 PIPE transaction, the Company used the relative fair value method to record the value of the warrants to the investors. Accordingly, \$1,164 of the proceeds has been attributed to such warrants and recorded as an increase to additional paid-in capital. In addition, the \$154 fair value of the warrants issued to the placement agent has been recorded as an increase to additional paid-in capital.

In connection with the August 2004 PIPE transaction, the Company issued 2,000,000 and 100,000 warrants with an exercise price of \$4.20 per share to the investors and to the placement agent, respectively. The exercise price of the warrants is subject to adjustment solely as a result of stock splits, recapitalizations and similar events. The fair value of the warrants was determined based on a fair market value of the Company's common stock of \$3.39 per share. As the shares of common stock were issued at a discount to their fair market value at the closing of the April 2004 PIPE transaction, the Company used the relative fair value method to record the value of the warrants to the investors. Accordingly, \$2,482 of the proceeds has been attributed to such warrants and recorded as an increase to additional paid-in capital. In addition, the \$239 fair value of the warrants issued to the placement agent has been recorded as an increase to additional paid-in capital.

Since the shares of common stock issued in the August 2004 PIPE transaction were sold at a price below the exercise price of the warrants issued in the October 2003 and April 2004 PIPE transactions, the exercise price of the common stock warrants granted to the investors and placement agent in the Company's October 2003 and April 2004 PIPE transactions has been adjusted to reflect the subsequent issuance of dilutive securities as provided for in the respective warrants. Accordingly, the exercise price of the warrants issued

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to the investors and placement agent in October 2003 has been adjusted from their original amounts of \$5.29 and \$6.86 per share to \$4.99 and \$6.24 per share, respectively. The exercise price of the warrants issued to the investors and placement agent in the April 2004 PIPE transaction has been adjusted from its original amount of \$5.30 per share to \$4.91 per share to \$5.07.

In 2004, the stockholders approved an increase in the number of “undesigned” shares that the Company is authorized to issue by 5,000,000 such that the total number of authorized “undesigned” shares following the effectiveness of such increase is 10,000,000 at December 31, 2004.

### 8. STOCK INCENTIVE PLAN

In October 2001, the Company’s Board of Directors adopted the Pro-Pharmaceuticals, Inc. 2001 Stock Incentive Plan (the “Incentive Plan”), which permits awards of incentive and nonqualified stock options and other forms of incentive compensation to employees and non-employees such as directors and consultants. The Board reserved 2,000,000 shares of common stock for issuance upon exercise of grants made under the Incentive Plan. Options granted under the Incentive Plan vest either immediately or over a period of up to three years, and expire 3 years to 10 years from the grant date. In 2004, the stockholders approved an increase in the number of shares of common stock subject to the Incentive Plan by 3,000,000 such that the total number of shares subject to awards under the Incentive Plan is 5,000,000. At December 31, 2005, there were 2,834,000 shares available for future grant under the Incentive Plan.

In 2003, the stockholders approved the Pro-Pharmaceuticals, Inc. 2003 Non-Employee Director Stock Option Plan (the “Director Plan”), which permits awards of stock options to non-employee directors. The stockholders reserved 1,000,000 shares of common stock for issuance upon exercise of grants made under the Director Plan. At December 31, 2005, there were 905,250 shares available for future grant under the Director Plan.

In addition, the Company has awarded 464,604 non-plan stock option grants to non-employees. The non-plan grants have vesting periods and expiration dates similar to those options granted under the Incentive Plan. All 464,604 non-plan grants are outstanding at December 31, 2005.

Information about all options granted and outstanding during these periods is as follows:

	Shares	Exercise Price Per Share	Weighted Average Exercise Price
Outstanding, January 1, 2004		2.92 – 4.05	3.76
Granted	2,225,604		
Cancelled	277,750 (100,000)	1.90 – 5.80 4.05	2.55 4.05
Outstanding, December 31, 2004	2,403,354	1.90 – \$ 5.80	\$ 3.61
Granted	272,000	2.61 – 5.16	3.31
Outstanding, December 31, 2005	2,675,354	1.90 – \$ 5.80	\$ 3.57

The following tables summarize information about stock options outstanding at December 31, 2005:

Exercise Price	Options Outstanding			Options Exercisable	
	Number of Shares	Weighted Average Remaining Contractual Life (Years)	Weighted Average Exercise Price	Number of Shares	Weighted Average Exercise Price
\$1.90 – \$2.82	365,000	9.01	\$ 2.28	71,667	\$ 1.90
\$2.61 – \$4.05	2,225,354	5.20	\$ 3.72	2,225,354	\$ 3.72
\$5.16 – \$5.80	85,000	1.25	\$ 5.35	85,000	\$ 5.35

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The 293,333 of unvested options at December 31, 2005 vest as follows: 121,667 in 2006, 121,666 in 2007 and 50,000 in 2008.

During 2001, the Company entered into a consulting agreement with a non-employee, who was also a Board member and former member of the Audit Committee, pursuant to which the Company granted 200,000 options to purchase common stock at an exercise price of \$3.50 in consideration for services to be performed. At the time of issuance, these options were valued at \$239 based on a deemed fair market value of the Company's common stock of \$2.28 per share. A portion of these options vested during fiscal years 2001 and 2002, and the remainder vested in 2003. The Company recorded fair value adjustments of \$28 and \$17 related to the unvested consultant options during 2003 and 2002, respectively. Total expense for the years ended December 31, 2003, 2002 and 2001 related to these options was \$72, \$64 and \$147, respectively.

In March 2002, the Company entered into a second agreement with the same non-employee, by which the Company granted 2,000 options a month to purchase common stock at an exercise price of \$3.50 in consideration for monthly consulting services. On November 11, 2002 such agreement was superceded by an amendment, which was effective retroactively to the date of the original agreement, March 1, 2002. Under the amended agreement, the Company granted 24,000 options on March 1, 2002, which vest at a rate of 2,000 options per month, as services are performed. These options were valued using the Black-Scholes option-pricing model, based on a deemed fair market value of the Company's common stock of \$3.50 per share. During 2002, the Company recorded a \$41 charge to stock compensation expense related to the 20,000 options that vested during the year under the amended agreement. As of December 31, 2002, the Company had deferred compensation of \$11 that related to the remaining unvested options, which was recognized in 2003.

In June 2003, the Company entered into a third agreement with the same non-employee, by which the Company granted 24,000 options effective retroactively to March 1, 2003, which vest at a rate of 2,000 options per month as services are performed. These options were valued using the Black-Scholes option-pricing model, based on a fair market value of the Company's common stock of \$3.50 per share. The consulting arrangement was concluded on March 1, 2004. The Company recorded fair value adjustments of (\$2) and \$21 related to the unvested consultant options during 2004 and 2003, respectively. Total expense for the years ended December 31, 2004 and 2003 related to these options was \$17 and \$40, respectively.

In January 2003, the Company granted 100,000 options at an exercise price of \$3.50 to a Board member for consulting services unrelated to services performed as a director. One-third of the options vested immediately and the balance vests in equal amounts on the first and second anniversaries of the award. The options were valued using the Black-Scholes option-pricing model, based on a fair market value of the Company's common stock of \$2.80 per share. The consulting services were completed and the consulting arrangement was concluded as of March 31, 2004. The Company recorded fair value adjustments of (\$5) and \$82 related to the unvested consultant options during 2004 and 2003, respectively. Total expense for the years ended December 31, 2004 and 2003 related to these options was \$51 and \$192, respectively.

In May 2003, the Company granted 10,000 options at an exercise price of \$3.50 to a new member of the Scientific Advisory Board. One-half of the options vested immediately and the balance vests on the second anniversary. These options were valued using the Black-Scholes option-pricing model based on a fair market value of the Company's common stock of \$2.80 per share. The Company recorded fair value adjustments of \$2 and \$6 related to the unvested consultant options during 2004 and 2003, respectively. Total expense for the years ended December 31, 2004 and 2003 related to these options was \$5 and \$13, respectively.

In September 2003, the Company granted 25,000 options each to a Board member and to a member of the Scientific Advisory Board for consulting services. The options were exercisable immediately at \$4.05 per

share. These options were valued using the Black-Scholes option-pricing model based on a deemed fair market value of the Company's common stock of \$4.05 per share. The Company recorded a \$122 charge to stock compensation expense in 2003 related to these awards.

In October 2003, in connection with the resignation of its former Chief Financial Officer, the Company accelerated the vesting on 100,000 options granted to such officer in September 2003 at an exercise price of \$4.05, which was equal to the fair market value of the common stock on the date of grant. As the fair market value of the common stock was \$4.45 per share at the time the vesting was accelerated, the Company recorded a \$40 charge to stock compensation expense as required under APB No. 25 and related interpretations. Also, in October 2003, such officer exercised on a cashless basis 50,000 options at an exercise price of \$2.97 per share. As the fair market value of the Company's common stock on the date of exercise was \$4.45 per share, the Company recorded a charge of \$74 to stock compensation expense in 2003 related to the exercise of these options.

In March 2004, the Company issued 25,000 options in fulfillment of a September 2003 agreement with an investor relations firm. The agreement obligated the Company to pay a monthly retainer and issue options at a rate of 5,000 options per month, up to a maximum of 100,000 options, exercisable at \$5.80 per share as services are performed. The Company concluded the engagement in February 2004. The options are exercisable immediately and expire on March 26, 2007. Accordingly, the Company recorded \$29 as stock compensation expense in 2003 on the 15,000 options that vested as of December 31, 2003 and an additional stock compensation expense of \$23 in 2004 on the 10,000 options that vested in January and February 2004. The stock compensation expense was determined based on a fair market value of the options when the options were earned.

In April 2004, the Company entered into an agreement with an investor relations firm. The agreement obligated the Company to pay a monthly retainer and issue options at a rate of 5,000 per month up to a maximum of 60,000 options exercisable at \$5.16 per share as services are performed. During 2004, 45,000 options were earned but not issued. During 2005 15,000 options were earned and the full 60,000 options were issued. Company recorded \$66 in 2004 and \$15 in 2005 as stock compensation expense related to this agreement. The stock compensation expense was determined based on the fair market value of the options when the options were earned. The options are exercisable immediately and expire three years from the agreement date.

In November 2005, the Company issued 5,000 options to a member of the Scientific Advisory Board for consulting services. The options were exercisable immediately at \$2.61 per share. These options were valued using the Black-Scholes option-pricing model based on a deemed fair market value of the Company's common stock of \$2.61 per share which was the fair market value at the date of the grant. The Company recorded a \$7 charge to stock compensation expense in 2005 related to this award.

## **9. COMMITMENTS AND CONTINGENCIES**

*Research and Development Commitments* – During March 2005, the Company entered into contracts with PRA International, Inc. ("PRA"), a clinical research organization, to assist with the Phase II clinical trials of the Company's DAVANAT<sup>®</sup> product in combination with 5-Fluorouracil. PRA will serve as the manager of the clinical trial including design, management and implementation. The Company's expenditure commitments under its PRA contract, terminable at any time upon 30 days' notice, represent approximately \$40. On February 1, 2006 the Company terminated its agreement with PRA. The Company does not expect this termination to affect the clinical trial.

*Lease Commitments* – The Company leases its facility under a non-cancelable operating lease that expires in May 2006. In connection with the operating lease, the Company has issued a letter of credit which is secured by restricted cash on deposit with the bank as a security deposit in the amount of \$21,933 which is renewed annually. Rent expense under this operating lease was \$111, \$110, \$110, and \$479 for the years

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ended December 2005, 2004, 2003 and the cumulative period from inception (July 10, 2000) to December 31, 2005, respectively. In October 2005, the Company entered into a non-cancelable operating lease for an automobile, which expires in October 2007. Expenses under this lease amounted to \$3 in 2005.

Future minimum payments under these leases as of December 31, 2005 are approximately \$59 and \$10 in 2006 and 2007 respectively.

*Contingency* – In January 2004, Dr. Platt, the Company’s Chairman and Chief Executive Officer, filed a lawsuit in Massachusetts Superior Court against GlycoGenesys, Inc. for various claims including breach of contract. In its filing in February 2004, GlycoGenesys asserted counterclaims against the Company and Dr. Platt alleging tortious interference and misappropriation of proprietary rights. The counterclaims seek monetary damages and injunctive relief related to the Company’s intellectual property. In March 2004, the Company and Dr. Platt answered the counterclaims and denied any liability. In June 2004, the Court allowed, without opposition, a motion of GlycoGenesys for leave to file a supplemental counterclaim against the Company for defamation and unfair competition. The Company and Dr. Platt intend to contest these counterclaims vigorously and believe they will ultimately prevail. However, if the Company does not prevail, there could be a material adverse impact on the financial position, results of operations or cash flows of the Company. On February 2, 2006, GlycoGenesys filed a voluntary petition for protection under Chapter 11 of the U.S. Bankruptcy Code, which stayed the counterclaim litigation proceedings.

Pursuant to Board approval, the Company has agreed to indemnify Dr. Platt for the expenses of his defense of the counterclaims, some of which may be recoverable under insurance. In 2005 the Company incurred approximately \$259 of expenses in connection with this defense. Through December 31, 2005 the Company has incurred cumulative expenses of approximately \$427 in connection with this defense. No amount, if any, potentially recoverable from the insurance company has been recorded at December 31, 2005.

On January 28, 2005, the Company filed a request with the U.S. Patent and Trademark Office (USPTO) for an inter partes re-examination of U.S. Patent No. 6,680,306 owned by GlycoGenesys, Inc. because the Company believes that the invention claimed in this patent is anticipated by other inventions (technically, “prior art”), including the Company’s U.S. Patent No. 6,645,946 for DAVANAT®. In an October 18, 2005 action, the USPTO agreed with the Company’s argument that all claims stated in the ‘306 patent are anticipated by prior art. On December 19, 2005, GlycoGenesys filed a response to the USPTO, and on January 18, 2006, the Company responded to the GlycoGenesys submission. The matter is now before the USPTO for a final decision. The Company believes that the USPTO actions to date support its belief that the invention claimed in the DAVANAT patent is prior art relative to the GlycoGenesys patent.

In the ordinary course of business, the Company may from time to time be involved in other legal matters that in the Company’s estimation will not have a material adverse impact on it. The Company records accruals for such contingencies to the extent that the Company concludes that their occurrence is probable and the related damages are estimable.

## 10. INCOME TAXES

The components of the net deferred tax assets are as follows at December 31:

	2005	2004
Operating loss carryforwards	\$ 9,178	\$ 6,551
Tax credit carryforwards	543	444
Other temporary differences	74	45
	<u>9,795</u>	<u>7,040</u>
Less valuation allowance	(9,795)	\$(7,040)
	<u>\$ —</u>	<u>\$ —</u>

As of December 31, 2005, the Company has federal and state net operating loss carryforwards totaling approximately \$22,894 and \$22,229, respectively, which expire through 2025. In addition, the Company has federal and state research and development and investment tax credits of approximately \$361 and \$182, respectively, which expire through 2020. If substantial changes in the Company's ownership should occur as defined by Section 382 of the Internal Revenue Code (the "Code"), there could be annual limitations on the amount of carryforwards which may be realized in future periods. Because of the Company's limited operating history and its recorded losses, management has provided a 100% allowance against the Company's net deferred tax assets.

#### **11. SUBSEQUENT EVENTS**

On February 14, 2006 the Company issued \$10,000 of 7% Convertible Debentures convertible, at the option of the holders, at any time into shares of the Company's common stock at a price of \$3.35 per share, and warrants to purchase an aggregate of approximately 1.5 million shares of the Common Stock at an exercise price of \$3.35 per share, to purchasers of this Debenture. The Warrants are exercisable beginning the 181<sup>st</sup> day after the agreement date and are exercisable for a period of five years from the date of issue. The initial conversion price of the Debentures and exercise price of the warrants equals 110% of the closing price of the Common Stock on the American Stock Exchange on the date of the Purchase Agreement (the "Agreement").

The conversion price and exercise price are each subject to certain anti-dilution protections, including for stock splits, stock dividends, change in control events and dilutive issuances of Common Stock or common stock equivalents at an effective price per share that is lower than the then conversion price. In the event of a dilutive issuance of common stock equivalents, the conversion price and exercise price would be reduced to equal the lower price per share of the subsequent transaction.

Under the terms of the Convertible Debentures, interest is payable monthly commencing July 1, 2006 and principal is payable in 18 equal monthly installments commencing August 1, 2006. Payments of principal and interest may be made in Common Stock or cash at the Company's option. Amounts paid in Common Stock must be paid at the lower of the then conversion price or 90% of the average of the 5 lowest value weighted average price for the 20 consecutive trading days prior to the payment. The Company may not make payments in the form of Common Stock if such payment would result in the cumulative issuance of Common Stock exceeding 19.999% of the Common Shares outstanding on the day immediately preceding the Agreement date, unless prior approval is obtained from a majority of shareholders. It is not known at this time if the Company will be required to issue in excess of 19.999% of currently outstanding Common Stock shares to satisfy its obligations under the Debentures because payments of principal and interest in the form of common stock are dependent on future share prices. As a precautionary measure, the Company plans to seek shareholder approval for the issuance of shares for this transaction, even though such approval may not be required. In connection with closing the transaction, the Company obtained agreements of holders of 42% of the Company's outstanding common stock to vote their shares to approve issuances of underlying shares that exceed the issuable maximum.

The Company is required to file a Registration Statement with the SEC within 30 calendar days after the February 14, 2006 closing of the transaction. If the Company fails to timely file the Registration Statement on time the Company will be required to pay each holder an amount, in cash, as partial liquidated damages and not as a penalty, equal to 2% of the aggregate principal amount of Debentures then held by such holder. The Agreement contains certain events of default under which not less than 130% of the outstanding principal amount of the Debenture plus all accrued and unpaid interest is immediately payable in cash. Events of default include among other things, failure to make payments of principal, or interest or liquidated damages and other amounts owing to a holder of any Debenture when due and payable which is not cured within 5 trading days, and failure to have the Registration Statement declared effective by the SEC within 180 calendar days after the closing date of the Agreement.

**12. SELECTED QUARTERLY FINANCIAL DATA (UNAUDITED)**

Summarized quarterly financial data for the last two years are as follows:

	<u>First Quarter</u>	<u>Second Quarter</u>	<u>Third Quarter</u>	<u>Fourth Quarter</u>
<b>2005</b>				
Operating expenses	\$ 1,453	\$ 1,728	\$ 1,705	\$ 1,769
Net loss	(1,417)	(1,698)	(1,680)	(1,749)
Net loss per share:				
Basic	(0.05)	(0.06)	(0.06)	(0.07)
Diluted	(0.05)	(0.06)	(0.06)	(0.07)
<b>2004</b>				
Operating expenses	\$ 1,874	\$ 1,437	\$ 1,799	\$ 2,194
Net loss	(1,854)	(1,405)	(1,763)	(2,158)
Net loss per share:				
Basic	(0.08)	(0.06)	(0.07)	(0.07)
Diluted	(0.08)	(0.06)	(0.07)	(0.07)

\* \* \* \* \*

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We consent to the incorporation by reference in Registration Statement Nos. 333-109887, 333-115118, 333-118907 and 333-111650 on Form S-3 and in Registration Statement Nos. 333-116629 and 333-109893 on Form S-8 of our report dated March 14, 2006, relating to the consolidated financial statements of Pro- Pharmaceuticals, Inc. appearing in this Annual Report on Form 10-K of Pro-Pharmaceuticals, Inc. for the year ended December 31, 2005.

/s/ Deloitte & Touche LLP

Boston, Massachusetts  
March 14, 2006

## Certification pursuant to Rule 13a-14(a) of the Securities Act of 1934

I, David Platt, certify that:

1. I have reviewed this annual report on Form 10-K of Pro-Pharmaceuticals, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and we have:
  - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) [Paragraph omitted in accordance with SEC transition instructions contained in SEC Release Nos. 34-47986 and 34-49313];
  - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 14, 2006

/s/ DAVID PLATT

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Name: David Platt  
Title: President and Chief Executive Officer  
(principal executive officer)

## Certification pursuant to Rule 13a-14(a) of the Securities Act of 1934

I, Carl Lueders, certify that:

1. I have reviewed this annual report on Form 10-K of Pro-Pharmaceuticals, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and we have:
  - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - b) [Paragraph omitted in accordance with SEC transition instructions contained in SEC Release Nos. 34-47986 and 34-49313];
  - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 14, 2006

/s/ CARL LUEDERS

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Name: Carl Lueders  
Title: Chief Financial Officer  
(principal financial and accounting officer)

**CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350,  
AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Pro-Pharmaceuticals, Inc. (the "Company") on Form 10-K for the period ended December 31, 2005 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, David Platt, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

- (1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Dated: March 14, 2006

/s/ David Platt

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Name: David Platt  
Title: President and Chief Executive Officer  
(principal executive officer)

A signed original of this written statement required by Section 906, or other document authenticating, acknowledging, or otherwise adopting the signature that appears in typed form within the electronic version of this written statement required by Section 906, has been provided to Pro-Pharmaceuticals, Inc. and will be retained by Pro-Pharmaceuticals, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.

**CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350,  
AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Pro-Pharmaceuticals, Inc. (the "Company") on Form 10-K for the period ended December 31, 2005 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Carl Lueders, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

- (1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Dated: March 14, 2006

/s/ Carl Lueders

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Name: Carl Lueders  
Title: Chief Financial Officer  
(principal financial and accounting officer)

A signed original of this written statement required by Section 906, or other document authenticating, acknowledging, or otherwise adopting the signature that appears in typed form within the electronic version of this written statement required by Section 906, has been provided to Pro-Pharmaceuticals, Inc. and will be retained by Pro-Pharmaceuticals, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.