

PRO PHARMACEUTICALS INC

Form 424B3

March 29, 2006

Table of Contents

Filed pursuant to Rule 424(b)(3)

Registration No. 333-132459

PROSPECTUS

PRO-PHARMACEUTICALS, INC.

7,300,000 Shares of Common Stock

This prospectus relates to the offer and sale from time to time by the selling security holders identified in this prospectus, and their pledgees, assignees and successors-in-interest, of (i) up to 5,150,000 shares of our common stock issuable upon conversions or redemptions of, or as interest payments on, an aggregate \$10,000,000 original principal amount of our 7% Convertible Debentures, and (ii) up to 2,150,000 shares of our common stock issuable upon the exercise of warrants. We are filing the registration statement of which this prospectus is a part in order to fulfill contractual obligations which we undertook at the time of the original issuance of the Debentures and warrants.

The prices at which such stockholders may sell the shares in this offering will be determined by the prevailing market price for the shares or in negotiated transactions. We will not receive any of the proceeds from the sale of the shares.

Our common stock is traded on the American Stock Exchange under the symbol PRW. On March 9, 2006, the last reported sale price of our common stock was \$3.75 per share. We urge you to obtain current market quotations for our common stock.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page 4.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is March 29, 2006.

Table of Contents

TABLE OF CONTENTS

<u>Prospectus Summary</u>	3
<u>About Pro-Pharmaceuticals, Inc.</u>	3
<u>Risk Factors</u>	4
<u>Special Note Regarding Forward-looking Statements</u>	8
<u>Use of Proceeds</u>	8
<u>Description of Transaction</u>	8
<u>Selling Stockholders</u>	9
<u>Plan of Distribution</u>	12
<u>Legal Matters</u>	14
<u>Experts</u>	14
<u>Where You Can Find More Information</u>	14
<u>Incorporation of Certain Documents by Reference</u>	14

Our executive offices are located at 189 Wells Avenue, Newton, Massachusetts 02459. Our telephone number is (617) 559-0033, fax number is (617) 928-3450, e-mail address is squeglia@pro-pharmaceuticals.com, and our website address is www.pro-pharmaceuticals.com. The information on our website is not incorporated by reference into this prospectus.

You should rely only on the information contained in this prospectus, including information incorporated by reference in this prospectus, or any supplement to which we have referred you. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus or any supplement is accurate as of any date other than the date on the front of those documents or that any document incorporated by reference is accurate as of any date other than its filing date. You should not consider this prospectus to be an offer or solicitation relating to the securities in any jurisdiction in which such an offer or solicitation relating to the securities is not authorized. Furthermore, you should not consider this prospectus to be an offer or solicitation relating to the securities if the person making the offer or solicitation is not qualified to do so, or if it is unlawful for you to receive such an offer or solicitation.

Table of Contents

PROSPECTUS SUMMARY

*This summary highlights important features of this offering and the information included or incorporated by reference in this prospectus. This summary does not contain all of the information that you should consider before investing in our common stock. You should read this prospectus and the information and documents incorporated by reference carefully. Such documents contain important information you should consider when making your investment decision. See *Incorporation of Certain Documents by Reference* on page 14.*

Unless the context otherwise requires, all references to we, our, our company, or the Company in this prospectus refer to Pro-Pharmaceuticals, Inc., a Nevada corporation, and its subsidiaries, and their respective predecessor entities for the applicable periods, considered as a single enterprise.

About Pro-Pharmaceuticals, Inc.

Pro-Pharmaceuticals, Inc. is engaged in the discovery, development and commercialization of carbohydrate-based therapeutic compounds. We believe our expertise in carbohydrates offer numerous opportunities to provide advanced treatment of disease including cancer, cardiovascular disease, inflammatory disease (including fibrosis and cirrhosis), Alzheimer's disease and viral infections.

Our work has initially concentrated on target delivery of chemotherapy drugs for the treatment of cancer. We believe our initial product candidate - DAVANAT® - when used in combination with existing FDA-approved cancer drugs may increase the efficacy and decrease the toxicity of current chemotherapy treatment.

DAVANAT® 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 trial. We have also 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 products are in the development stage.

The Offering

Common stock offered by selling stockholders	7,300,000 shares
Use of proceeds	We will not receive any proceeds from the sale of shares in this offering.
American Stock Exchange symbol	PRW

Table of Contents

RISK FACTORS THAT MAY AFFECT FUTURE RESULTS

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, Inc.

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

We Have Incurred Net Losses to Date and Depend on Outside Capital. Our accumulated deficit as of December 31, 2005 was \$26,430,000. 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 \$4,466,000 of available cash and cash equivalents as of December 31, 2005, and the approximately \$9.3 million of net proceeds from the sale of 7% Convertible Debentures and Common Stock Purchase Warrants 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

Table of Contents

regulatory approval process, selling pharmaceutical products, or negotiating, establishing and maintaining strategic relationships. Any growth of our company will require us to expand our management and our operational and financial systems and controls. If we are unable to do so, our business and financial condition would be materially harmed. If rapid growth occurs, it may strain our operational, managerial and financial resources.

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

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

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 \$250,000, ineligibility of our stock for listing or 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 hereunder 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. Please see Description of Transaction below for additional detail about the Debentures and warrants.

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

Table of Contents

could reject an application or require us to conduct additional clinical or other studies as part of the regulatory review process. Delays in obtaining or failure to obtain FDA approvals would prevent or delay the commercialization of our products, which would prevent, defer or decrease our receipt of revenues. If we receive initial regulatory approval, our product candidates will be subject to extensive and rigorous ongoing domestic and foreign government regulation.

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

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

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

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

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

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

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

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

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

Table of Contents

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. In the registration statement of which this prospectus is a part, 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.

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.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference contain, in addition to historical information, forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements relate to future events or our future financial performance and can be identified by the use of forward-looking terminology such as may, could, expect, anticipate, estimate, continue or other similar words. 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, those described in the Risk Factors section of this prospectus. We cannot assure you that we have identified all the factors that create uncertainties. Readers should not place undue reliance on forward-looking statements. We undertake no obligation to publicly release the result of any revision of these forward-looking statements to reflect events or circumstances after the date they are made or to reflect the occurrence of unanticipated events.

USE OF PROCEEDS

The proceeds from the sale of each selling stockholder's shares of common stock will belong to that selling stockholder. We will not receive any proceeds from those sales.

DESCRIPTION OF TRANSACTION

On February 14, 2006, we completed a financing in which we issued an aggregate \$10 million original principal amount of 7% Convertible Debentures due February 14, 2008 (the Debentures), convertible at any time at a holder's option into shares of our common stock at a price of \$3.35 per share, subject to adjustment, and warrants to purchase approximately 1.5 million shares of our common stock at an initial exercise price of \$3.35 per share, subject to adjustment. The initial conversion price of the Debentures and exercise price of the warrants equaled 110% of the closing price of our common stock on the American Stock Exchange on the date we completed the transaction. We are required on behalf of the holders of these securities (i) to register the shares of common stock issuable upon conversion or redemption of, or payable as interest on, the Debentures, or upon exercise of the Warrants (all of such shares, collectively, the Underlying Shares), and (ii) to seek approval of our shareholders, pursuant to the rules of the American Stock Exchange, to issue Underlying Shares in excess of 19.999% (the Issuable Maximum) of the number of the issued and outstanding shares of our common stock on the date we sold these securities. Because the number of Underlying Shares issuable pursuant to the Debentures and Warrants is based on the future prices of our common stock, we do not know at this time if we will be required to issue a number of Underlying Shares that exceed the Issuable Maximum. As a precautionary measure, we plan to seek the approval of our shareholders for us to issue Underlying Shares that exceed the Issuable Maximum, even though such approval may not be required. In connection with closing the transaction, we obtained agreements of holders of 42% of our outstanding common stock to vote their shares to approve issuances of Underlying Shares that exceed the Issuable Maximum.

Summary of Certain Terms of the Debentures

The conversion price of the Debentures is subject to adjustments for (i) stock splits, stock dividends, combinations, reclassifications, mergers, consolidations, distributions of assets or evidence of indebtedness, sales or transfers of substantially all assets, share exchanges or similar events, and (ii) dilutive issuances of common stock, or securities convertible, exercisable or exchangeable for shares of our common stock (Common Stock Equivalents), at an effective price per share that is lower than the then conversion price, such adjustment to result in a full-ratchet reduction of the conversion price to the price per share sold in the dilutive issuance. The Debentures require payment of interest on the outstanding principal amount at the rate of 7% per annum beginning July 1, 2006 and thereafter at each monthly redemption of principal, each conversion, and the maturity date of the Debentures, in cash or, if we have procured shareholder approval for issuances in excess of the Issuable Maximum, shares of common stock. Interest paid in shares of common stock is paid at the lesser of the then conversion price or the average of the 5 lowest volume weighted average prices (VWAP) for the common stock on the American Stock Exchange during the 20 consecutive trading days immediately prior to the applicable interest payment date.

We are required to redeem the Debentures in 18 equal monthly installments beginning August 1, 2006. The monthly redemption amounts may be paid in shares of common stock up to the Issuable Maximum, and must be paid in cash thereafter unless we receive shareholder approval to issue shares in excess of the Issuable Maximum. Redemptions paid in shares must be paid at a price equal to the lesser of the then conversion price or 90% of the average of the 5 lowest VWAPs for our common stock on the American Stock Exchange during the 20 consecutive trading days prior to the applicable redemption payment. We may not redeem the Debentures in shares unless certain conditions are met, some of which are that we have timely paid all amounts due under the Debentures, no other

Table of Contents

specified event of default thereunder has occurred, and that the Underlying Shares are registered for resale. If an event of default occurs under the Debentures, we must pay to the holders, in cash, an amount that is equal to the sum of (i) at least 130% of the outstanding principal and all accrued and unpaid interest thereon, and (ii) any amounts then otherwise due to the holders. As long as at least 10% in original principal amount of Debentures remains outstanding, we may not take certain actions, including incurrence of indebtedness beyond stated limits, amendments of governance documents, payments of dividends or distributions, and repurchases of more than a de minimis number of shares of common stock or Common Stock Equivalents.

Summary of Certain Terms of the Warrants

The warrants are exercisable in cash to purchase shares of our common stock beginning the 181st day after, and until the fifth anniversary of, the date of issue. The exercise price of the warrants shall be adjusted in the event of (i) stock splits, stock dividends, combinations, reclassifications, mergers, consolidations, distributions of assets or evidence of indebtedness, sales or transfers of substantially all assets, share exchanges or similar events, and (ii) dilutive issuances of common stock or Common Stock Equivalents at an effective price per share that is lower than the then exercise price, such adjustment to result in a full-ratchet reduction of the exercise price to the price per share sold in the dilutive issuance.

Copies of the Debentures and Warrants were filed as Exhibits 10.25 and 10.28 to our Annual Report on Form 10-K for the year ended December 31, 2005 filed with the SEC on March 15, 2006, which is incorporated herein by reference. The summary of the matters set forth above is qualified in its entirety by reference to such exhibits.

SELLING STOCKHOLDERS

This prospectus relates to the resale from time to time of up to a total of 7,300,000 shares of our common stock by the selling stockholders, comprising:

5,150,000 shares of common stock issuable upon conversion or redemption of, or as interest payments on, the Debentures;

1,950,000 shares of common stock issuable upon exercise of warrants; and

200,000 shares of common stock issuable upon exercise of a warrant issued to the placement agent as partial compensation for services rendered to us as placement agent for the financing described in this prospectus.

We issued the Debentures and warrants on February 14, 2006 to institutional investors named in the table below in a private placement exempt from the registration requirements of the Securities Act of 1933, as amended. Pursuant to a contemporaneous Registration Rights Agreement with these investors, we agreed to file a registration statement, of which this prospectus is a part, with the SEC to register the resale of the shares of our common stock issuable under the Debentures and the warrants, and to keep the registration statement effective until the date when all of the shares registered hereunder are sold or the date on which the shares registered hereunder can be sold without registration and without restriction as to the number of shares that may be sold.

Table of Contents

The following table, based upon information currently known by us, sets forth as of February 14, 2006: (i) the number of shares held of record or beneficially by the selling stockholders as of such date, (ii) the number of shares that may be offered under this prospectus, and (iii) a footnote reference to any material relationship between Pro-Pharmaceuticals and the selling stockholder, if any. Beneficial ownership includes shares of common stock plus any securities held by the holder exercisable for or convertible into shares of common stock within sixty (60) days after February 14, 2006, in accordance with Rule 13d-3(d)(1) under the Securities Exchange Act of 1934, as amended. In addition, notwithstanding the sixty-day calculation period under Rule 13d-3(d)(1), for purposes of computing the beneficial ownership of the selling stockholders listed below, we have included the shares issuable upon exercise of the warrants issued to the selling stockholders on February 14, 2006 as described above (such shares, the Deemed Outstanding Warrant Shares) even though these warrants are not exercisable until August 14, 2006. None of the selling stockholders is a broker-dealer or an affiliate of a broker-dealer.

Name of Selling Stockholder	Common Stock Beneficially Owned Prior to the Offering (1)	Common Stock Issuable Upon Conversion or Redemption of, or as Interest on, 7% Convertible Debentures, or on Exercise of Warrants, Offered Pursuant to this Prospectus (2)	Common Stock Owned Upon Completion of this Offering (3)(4)	Percentage of Common Stock Owned Upon Completion of this Offering
Alexandra Global Master Fund Ltd. (5)	710,000	710,000	0	*
Bristol Investment Fund, Ltd. (6)	866,429	710,000	156,429	*
Cranshire Capital, L.P. (7)	955,874	710,000	245,874	*
DKR Soundshore Oasis Holding Fund Ltd. (8)	710,000	710,000	0	*
Iroquois Master Fund Ltd. (9)	710,000	710,000	0	*
JMG Capital Partners, L.P. (10)	355,000	355,000	0	*
JMG Triton Offshore Fund, Ltd. (11)	355,000	355,000	0	*
UBS Securities LLC f/b/o Kings Road Investments, Ltd. (12)	1,420,000	1,420,000	0	*
Smithfield Fiduciary, LLC (13)	1,536,667	1,420,000	116,667	*
Rodman & Renshaw Opportunity Fund, L.P. (14)	460,202	200,000	260,202	*
TOTAL	8,079,172	7,300,000	779,172	2.8%

* Amount less than one percent.

For each selling stockholder, the table above assumes the sale by that selling stockholder of all of its shares of common stock available for resale under this prospectus. Percentage calculations are based on 27,315,411 shares of our common stock issued and outstanding as of March 9, 2006.

Table of Contents

- (1) Includes (a)(i) shares issuable upon conversion or redemption of, and as interest payments on, the 7% Convertible Debentures issued and sold to the selling stockholders (collectively, the Debenture Shares), and (ii) Deemed Outstanding Warrant Shares; and (b) as applicable, shares issuable upon exercise of (i) currently exercisable warrants, which shares are registered for resale and subject to a prospectus filed September 24, 2004 (SEC file no. 333-118907) covering all shares issuable upon exercise of warrants disclosed therein (collectively, the September 2004 Warrant Shares), (ii) currently exercisable warrants, which shares are registered for resale and subject to a prospectus filed May 13, 2004 (SEC file no. 333-115118) covering all shares issuable upon exercise of the warrants as disclosed therein (collectively, the May 2004 Warrant Shares), and (iii) currently exercisable warrants, which shares are registered for resale and subject to a prospectus filed November 14, 2003 (SEC file no. 333-109887) covering all shares issuable upon exercise of the warrants as disclosed therein (collectively, the November 2003 Warrant Shares).
- (2) Each entry in the column represents, for the respective selling stockholder, the sum of Debenture Shares and Deemed Outstanding Warrant Shares.
- (3) Assumes solely for purpose of this table that such shares are still owned upon completion of the offering, which assumption is not intended to override the selling stockholder table in, as applicable, the prospectus covering the November 2003 Warrant Shares, the May 2004 Warrant Shares or the September 2004 Warrant Shares.
- (4) We do not know when or in what amounts a selling stockholder may offer shares for sale. The selling stockholders may not sell any or all of the shares offered by this prospectus. Because the selling stockholders may offer some or all of the shares pursuant to this offering, and because there are currently no agreements, arrangements or understandings with respect to any of the shares, we cannot estimate the number of the share that will be held by the selling stockholders after completion of the offering. However, for purposes of this table, we have assumed that, after completion of the offering, none of the shares covered by this prospectus will be held by the selling stockholders.
- (5) Includes (i) 515,000 Debenture Shares and (ii) 195,000 Deemed Outstanding Warrant Shares. Alexandra Investment Management, LLC, a Delaware limited liability company (Alexandra), serves as investment adviser to Alexandra Global Master Fund Ltd., a British Virgin Islands company (Master Fund). By reason of such relationship, Alexandra may be deemed to share dispositive power over the shares of common stock stated as beneficially owned by Master Fund. Alexandra disclaims beneficial ownership of such shares of common stock. Messrs. Mikhail A. Filimonov (Filimonov) and Dimitri Sogoloff (Sogoloff) are managing members of Alexandra. By reason of such relationship, Filimonov and Sogoloff may be deemed to share dispositive power over the shares of common stock stated as beneficially owned by Master Fund. Filimonov and Sogoloff disclaim beneficial ownership of such shares of common stock.
- (6) Includes (i) 515,000 Debenture Shares, (ii) 195,000 Deemed Outstanding Warrant Shares, (iii) 100,000 September 2004 Warrant Shares, (iv) 35,000 May 2004 Warrant Shares, and (v) 21,429 November 2003 Warrant Shares.
- (7) Includes (i) 515,000 Debenture Shares, (ii) 195,000 Deemed Outstanding Warrant Shares, (iii) 100,000 September 2004 Warrant Shares, (iv) 74,445 May 2004 Warrant Shares, and (v) 71,429 November 2003 Warrant Shares. Downsvew Capital, Inc. (Downsvew), of which Mitchell P. Kopin is President, is the general partner of Cranshire Capital L.P. and has the power to vote or dispose of the shares. Each of Downsvew and Mr. Kopin disclaims beneficial ownership of the shares.
- (8) Includes (i) 515,000 Debenture Shares and (ii) 195,000 Deemed Outstanding Warrant Shares. The investment manager of DKR Soundshore Oasis Holding Fund Ltd. (the Fund) is DKR Oasis Management Company LP (the Investment Manager). The Investment Manager has the authority to do any and all acts on behalf of the Fund, including voting any shares held by the Fund. Mr. Seth Fischer is the managing partner of Oasis Management Holding LLC, one of the general partners of the Investment Manager. Mr. Fischer has ultimate responsibility for trading with respect to the Fund. Mr. Fischer disclaims beneficial ownership of the shares.
- (9) Includes (i) 515,000 Debenture Shares and (ii) 195,000 Deemed Outstanding Warrant Shares. Joshua Silverman, the general partner of Iroquois Capital LP, may be deemed to have voting and dispositive over the shares of common stock. Mr. Silverman disclaims beneficial

ownership of such shares.

- (10) Includes (i) 257,500 Debenture Shares and (ii) 97,500 Deemed Outstanding Warrant Shares. JMG Capital Partners, L.P. is a California limited partnership (JMG Partners). Its general partner is JMG Capital Management, LLC, a

Table of Contents

Delaware limited liability company (the **Manager**), and an investment adviser that has voting and dispositive control over the investments of JMG Partners, including the shares of common stock offered by this prospectus. The equity interests of the Manager are owned by JMG Capital Management, Inc., a California corporation (**JMG Capital**), and Asset Alliance Holding Corp., a Delaware corporation. Jonathan M. Glaser is the Executive Officer and Director of JMG Capital and has sole investment discretion over the portfolio holdings of JMG Partners.

- (11) Includes (i) 257,500 Debenture Shares and (ii) 97,500 Deemed Outstanding Warrant Shares. JMG Triton Offshore Fund, Ltd., organized under the law of the British Virgin Islands (the **Fund**), is an international business company. The Fund's investment manager is Pacific Assets Management LLC, a Delaware limited liability company (the **Manager**), that has voting and dispositive control of the Fund's investments, including the shares of common stock offered by this prospectus. The equity interests of the Manager are owned by Pacific Capital Management, Inc., a California corporation (**Pacific**), and Asset Alliance Holding Corp., a Delaware corporation. The equity interests of Pacific are owned by Messrs. Roger Richter, Jonathan M. Glaser and Daniel A. David. Messrs. Glaser and Richter have sole investment discretion over the Fund's portfolio holdings.
- (12) Includes (i) 1,030,000 Debenture Shares and (ii) 390,000 Deemed Outstanding Warrant Shares. Kings Road Investments Ltd. (**Kings Road**) is a wholly-owned subsidiary of Polygon Global Opportunities Master Fund (**Master Fund**). Polygon Investment Partners LLP and Polygon Investment Partners LP (the **Investment Managers**), Polygon Investments Ltd. (the **Manager**), the Master Fund, Alexander Jackson, Reade Griffith and Paddy Dear share voting and dispositive power over the securities held by Kings Road including the shares offered under this prospectus. The Investment Managers, the Manager and Messrs. Jackson, Griffith and Dear disclaim beneficial ownership of the securities held by Kings Road.
- (13) Includes (i) 1,030,000 Debenture Shares, (ii) 390,000 Deemed Outstanding Warrant Shares, and (iii) 116,667 September 2004 Warrant Shares. Highbridge Capital Management, LLC (**Highbridge**) is the trading manager of Smithfield Fiduciary LLC (**Smithfield**) and has voting control and investment discretion over securities held by Smithfield. Glen Dubin and Henry Swieca control Highbridge. Each of Highbridge and Messrs. Dubin and Swieca disclaims beneficial ownership of the securities held by Smithfield.
- (14) Includes (i) 200,000 Deemed Outstanding Warrant Shares, (ii) 132,667 September 2004 Warrant Shares, (iii) 61,806 May 2004 Warrant Shares, and (iv) 65,729 November 2003 Warrant Shares.

PLAN OF DISTRIBUTION

Each selling stockholder of our common stock and any of their pledgees, assignees and successors-in-interest may, from time to time, sell any or all of its shares of common stock on the American Stock Exchange or any other stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices. A selling stockholder may use any one or more of the following methods when selling shares:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

privately negotiated transactions;

settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part;

broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;

Table of Contents

through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;

a combination of any such methods of sale; or

any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares under Rule 144 under the Securities Act of 1933, as amended (the "Securities Act"), if available, rather than under this prospectus.

Broker-dealers engaged by the selling stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with NASDR Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with NASDR IM-2440.

In connection with the sale of the common stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of the common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The selling stockholders and any broker-dealers or agents that are involved in selling the shares may be deemed to be "underwriters" within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Each selling stockholder has informed us that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the common stock. In no event shall any broker-dealer receive fees, commissions and markups which, in the aggregate, would exceed eight percent (8%).

We are required to pay certain fees and expenses incurred by us incident to the registration of the shares. We have agreed to indemnify the selling stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

Because selling stockholders may be deemed to be "underwriters" within the meaning of the Securities Act, they will be subject to the prospectus delivery requirements of the Securities Act including Rule 172 thereunder. In addition, any securities covered by this prospectus which qualify for sale pursuant to Rule 144 under the Securities Act may be sold under Rule 144 rather than under this prospectus. There is no underwriter or coordinating broker acting in connection with the proposed sale of the resale shares by the selling stockholders.

We agreed to keep this prospectus effective until the earlier of (i) the date on which the shares may be resold by the selling stockholders without registration and without regard to any volume limitations by reason of Rule 144(k) under the Securities Act or any other rule of similar effect or (ii) all of the shares have been sold pursuant to this prospectus or Rule 144 under the Securities Act or any other rule of similar effect. The resale shares will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the resale shares may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), any person engaged in the distribution of the resale shares may not simultaneously engage in market making activities with respect to the common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the selling stockholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of shares of the common stock by the selling stockholders or any other person. We will make copies of this prospectus

Table of Contents

available to the selling stockholders and have informed them of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

LEGAL MATTERS

The validity of the shares of common stock being offered hereby has been passed upon for Pro-Pharmaceuticals, Inc. by Greenberg Traurig, LLP of Boston, Massachusetts.

EXPERTS

The financial statements incorporated in this prospectus by reference from our Annual Report on Form 10-K for the year ended December 31, 2005, have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference, and have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission. You may read and copy any document we file with the SEC at the Public Reference Room (Room 1580), 100 F Street, N.W., Washington, D.C. 20549. You may also obtain information on the operations of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains a website (www.sec.gov) that contains the reports, proxy and information statements, and other information that we file electronically with the SEC.

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC. The registration statement contains more information than this prospectus regarding us and the securities, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC at the above address or from the SEC's Internet site.

Our worldwide web address is www.pro-pharmaceuticals.com. We have not incorporated by reference into this prospectus the information on our website, and you should not consider it to be a part of this document. Our web address is included in this document as an inactive textual reference only.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference information contained in documents that we file with the SEC, which means that we can disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings we will make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 prior to the termination of this offering:

- (1) Our Annual Report on Form 10-K for the year ended December 31, 2005, filed with the SEC on March 15, 2006;
- (2) Our Current Report on Form 8-K filed with the SEC on February 15, 2006;
- (3) Our Current Report on Form 8-K filed with the SEC on March 10, 2006;
- (4) All our filings pursuant to the Securities Exchange Act of 1934 after the date of filing the initial registration statement and prior to effectiveness of the registration statement; and

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- (5) The description of our common stock contained in our registration statement on Form 8-A filed with the SEC on September 9, 2003, including any amendments or reports filed for the purpose of updating that description.

You may request, orally or in writing, a copy of these documents, which will be provided to you at no cost, by contacting:

Pro-Pharmaceuticals, Inc.

189 Wells Avenue

Newton, Massachusetts 02459

Attention: Anthony D. Squeglia, Vice President, Investor Relations

Tel.: (617) 559-0033

E-mail: squeglia@pro-pharmaceuticals.com