

PRO-PHARMACEUTICALS, INC.

4,100,000 Shares of Common Stock \$.001 par value

This prospectus relates to the offer and sale from time to time of up to 2,000,000 shares of our outstanding common stock, and up to 2,100,000 shares of our common stock issuable upon the exercise of warrants, which are held by certain selling stockholders named in this prospectus.

The prices at which such stockholders and warrant holders 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 listed on the American Stock Exchange under the symbol "PRW." On September 7, 2004, the last reported sale price of our common stock was \$3.02 per share.

See "Risk Factors" beginning on page 3 to read about the risks you should consider carefully before buying shares of our common stock.

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 September 24, 2004.

[Table of Contents](#)

TABLE OF CONTENTS

About This Prospectus	2
About Pro-Pharmaceuticals, Inc.	2
Risk Factors	3
Forward-looking Statements	9
Use of Proceeds	9
Selling Stockholders	9
Plan of Distribution	13
Legal Matters	14
Experts	14
Where You Can Find More Information	14
Incorporation of Certain Documents by Reference	15

ABOUT THIS PROSPECTUS

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 15. 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.

ABOUT PRO-PHARMACEUTICALS, INC.

We are a development-stage pharmaceutical company that intends to identify, develop and seek regulatory approval of drugs and compositions that will reduce toxicity and improve the efficacy of currently existing chemotherapy drugs by reformulating or chemically upgrading the drugs with our proprietary carbohydrate technology. Our fundamental objective is to increase the body’s tolerance to the drugs by enabling targeted delivery of the drugs in order to protect healthy tissue. Our TargetDelivery™ technology could also permit higher doses of the chemotherapy drugs because current dosage levels are generally limited so as to avoid overly toxic effects on healthy cells. Our carbohydrate-based drug targeting and delivery system may also have applications for drugs used to treat other diseases and chronic health conditions.

The U.S. Food and Drug Administration in 2002 approved our Investigational New Drug application (“IND”) for DAVANAT®, which enabled us to undertake human clinical trials with our first drug delivery product. In February 2003, we began the Phase I clinical trial of DAVANAT® alone and co-administered with the proven chemotherapeutic drug, 5-Fluorouracil (in combination with our product, referred to as DAVANAT®-1), and announced the interim results in June 2004. We are in the sixth and final cohort of Phase I for DAVANAT®-1.

In January 2004, we announced the initiation of Phase II clinical trials of DAVANAT®-1 in cancer patients. This trial is part of a multi-center, open-label, single dose level study in patients with metastatic colorectal cancer who have failed standard chemotherapeutic regimens.

We are currently conducting preclinical animal experiments with additional IND candidates. We have not yet generated operating revenues.

[Table of Contents](#)

We were incorporated in January 2001. Our common stock trades on the American Stock Exchange under the symbol "PRW". Our address is 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.

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 contained in this prospectus 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 which 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 part or all of your investment.

Risks Related to Pro-Pharmaceuticals

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 June 30, 2004 was approximately \$15,965,000. 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

[Table of Contents](#)

favorable terms or at all. If adequate funds are not otherwise available, we may curtail operations significantly. 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 the \$8,776,000 of cash and cash equivalents on hand as of June 30, 2004, and the net proceeds of approximately \$5,500,000 realized from our private equity offering closed on August 12, 2004, we believe we have sufficient cash to fund our operations through at least December 31, 2005.

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

We Have Only Recently Begun 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 and 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 no direct experience in manufacturing or procuring products in commercial quantities, conducting other later-stage phases of the regulatory approval process, selling pharmaceutical products or licensing our technology, 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.

[Table of Contents](#)

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 continue to develop relationships with manufacturers and enter into collaborative arrangements with licensees or have others manufacture our products on a contract basis. We will 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 no direct 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 (on a consulting basis) and member of our Scientific Advisory Board; 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 Have Been Named 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 names 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. On June 15, 2004, the court allowed, without opposition, a motion of GlycoGenesys for leave to file a supplemental counterclaim for defamation and unfair competition against us. 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.

Risks Related to the Drug Development Industry

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

[Table of Contents](#)

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 the 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 have been named as a counterclaim defendant in a lawsuit instituted by Dr. Platt. See “Risks Related to Pro-Pharmaceuticals” above.

Our Products Could Infringe The Intellectual Property Rights Of 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

[Table of Contents](#)

are rapidly evolving. Our competitors include major, multinational pharmaceutical and chemical companies, specialized biotechnology firms and universities and other research institutions. Many of these competitors have greater financial and other resources, larger research and development staffs and more effective marketing and manufacturing organizations, than we do. In addition, academic and government institutions are increasingly likely to enter into exclusive licensing agreements with commercial enterprises, including our competitors, to market commercial products based on technology developed at such institutions. Our competitors may succeed in developing or licensing technologies and products that are more effective or less costly than ours, or succeed in obtaining FDA or other regulatory approvals for product candidates before we do.

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

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

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

Risks Related to Our Stock

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

[Table of Contents](#)

Large Sales Could Reduce The Trading Price Of Our Common Stock. We listed our common stock on the American Stock Exchange in September 2003. Accordingly, there is a limited history of trading of our stock on a national exchange and, based on varying trading volume to date, our stock could be considered “thinly traded.” In late 2003, on behalf of certain of our stockholders, we registered 11,358,835 shares of our common stock and 832,635 shares of stock issuable upon exercise of immediately exercisable warrants. In May 2004, we registered an additional 1,286,111 shares of common stock and 679,862 shares of stock issuable upon exercise of immediately exercisable warrants on behalf of certain of our stockholders. On September 24, 2004 we registered 2,000,000 shares of common stock and 2,100,000 shares of common stock issuable upon exercise of warrants issued in a private placement we completed on August 12, 2004. 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. We sold shares of common stock and warrants to purchase common stock in October 2003, April 2004 and August 2004 to investors who, as an incentive to purchase our securities in private placements, required us promptly to register their shares (including shares issuable upon exercise of the warrants) for resale 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 43% 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, including rule changes adopted by stock exchanges in connection with such legislation, 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 potential changes to currently accepted accounting practices, including the expensing of

[Table of Contents](#)

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.

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 common stock will belong to that selling stockholder. We will not receive any proceeds from those sales.

SELLING STOCKHOLDERS

This prospectus relates to the resale from time to time of up to a total of 4,100,000 shares of our common stock by the selling stockholders, comprising:

- 2,000,000 shares of common stock;
- 2,000,000 shares of common stock issuable upon exercise of warrants, with an exercise price of \$4.20 per share; and
- 100,000 shares of common stock issuable upon exercise of a warrant with an exercise price of \$4.20 per share, issued to Rodman & Renshaw LLC as partial compensation for services rendered to us as placement agent for the financing described below.

We issued 2,000,000 shares and 2,100,000 warrants on August 12, 2004 to institutional investors named in the table below in a private placement exempt from the registration requirements of the Securities Act. Pursuant to a Registration Rights Agreement dated August 12, 2004, we agreed to file this registration statement, of which this prospectus is a part, with the

[Table of Contents](#)

SEC, to register the resale of the shares of our common stock we issued, and which we will issue upon exercise of warrants, to those stockholders 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.

The following table, based upon information currently known by us, sets forth as of August 12, 2004: (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 the date of this prospectus, 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 and to Rodman & Renshaw LLC on August 12, 2004 as described above (such shares, the “Deemed Outstanding Warrant Shares”) even though these warrants are not exercisable until February 13, 2005. The Deemed Outstanding Warrant Shares are also included in the shares of common stock being offered pursuant to this prospectus as shown in the following table and footnotes.

Name of Selling Stockholder	Common Stock Owned Prior to the Offering	Common Stock Being Offered Pursuant to this Prospectus	Common Stock Owned Upon Completion of this Offering	Percentage of Common Stock Owned Upon Completion of this Offering
Alpha Capital AG ⁽¹⁾	292,143	200,000	92,143	*
Basso Equity Opportunity Holding Fund Ltd. ⁽²⁾	127,500	110,000	17,500	*
Basso Multi-Strategy Holding Fund Ltd. ⁽³⁾	407,500	390,000	17,500	*
Bristol Investment Fund, Ltd. ⁽⁴⁾	326,429	200,000	126,429	*
Cordillera Fund, LP ⁽⁵⁾	66,666	66,666	0	*
Cranshire Capital, L.P. ⁽⁶⁾	345,874	200,000	145,874	*
Crescent International Ltd. ⁽⁷⁾	273,100	134,000	139,100	*
F. Berdon Co. LP ⁽⁸⁾	34,000	34,000	0	*
Gryphon Master Fund, LP ⁽⁹⁾	449,763	200,000	249,763	*
ITF, LTD, Mauritius ⁽¹⁰⁾	100,000	100,000	0	*
Omicron Master Trust ⁽¹¹⁾	795,238	666,666	128,572	*
Portside Growth and Opportunity Fund ⁽¹²⁾	302,915	200,000	102,915	*
PROLATE LLC ⁽¹³⁾	166,666	166,666	0	*
R&R Opportunity Fund LP ⁽¹⁴⁾	65,334	65,334	0	*

[Table of Contents](#)

Name of Selling Stockholder	Common Stock Owned Prior to the Offering	Common Stock Being Offered Pursuant to this Prospectus	Common Stock Owned Upon Completion of this Offering	Percentage of Common Stock Owned Upon Completion of this Offering
Silver Oak Investments, Inc. ⁽¹⁵⁾	200,000	200,000	0	*
Smithfield Fiduciary LLC ⁽¹⁶⁾	233,334	233,334	0	*
SRG Capital, LLC ⁽¹⁷⁾	166,666	166,666	0	*
Stonestreet, LP ⁽¹⁸⁾	327,777	300,000	27,777	*
TCMP ³ Partners ⁽¹⁹⁾	121,429	100,000	21,429	*
The Tail Wind Fund Limited ⁽²⁰⁾	337,383	266,668	70,715	*
Rodman & Renshaw LLC ⁽²¹⁾	227,535	100,000	127,535	*
TOTAL	5,367,252	4,100,000	1,267,252 ⁽²²⁾	4.5%

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 August 12, 2004.

- ⁽¹⁾ Includes (i) 100,000 Deemed Outstanding Warrant Shares, (ii) 35,000 shares issuable upon exercise of 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) 57,143 shares issuable upon exercise of 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⁾ Includes 55,000 Deemed Outstanding Warrant Shares and 17,500 May 2004 Warrant Shares.
- ⁽³⁾ Includes 195,000 Deemed Outstanding Warrant Shares and 17,500 May 2004 Warrant Shares.
- ⁽⁴⁾ Includes 100,000 Deemed Outstanding Warrant Shares, 35,000 May 2004 Warrant Shares and 21,429 November 2003 Warrant Shares.
- ⁽⁵⁾ Includes 33,333 Deemed Outstanding Warrant Shares.
- ⁽⁶⁾ Includes 100,000 Deemed Outstanding Warrant Shares, 74,445 May 2004 Warrant Shares and 71,429 November 2003 Warrant Shares.
- ⁽⁷⁾ Includes 67,000 Deemed Outstanding Warrant Shares, 45,000 May 2004 Warrant Shares and 43,000 November 2003 Warrant Shares.
- ⁽⁸⁾ Includes 17,000 Deemed Outstanding Warrant Shares.

Table of Contents

- ⁽⁹⁾ Includes 100,000 Deemed Outstanding Warrant Shares, 69,445 May 2004 Warrant Shares and 71,429 November 2003 Warrant Shares.
- ⁽¹⁰⁾ Includes 50,000 Deemed Outstanding Warrant Shares.
- ⁽¹¹⁾ Includes 333,333 Deemed Outstanding Warrant Shares, 100,000 May 2004 Warrant Shares and 28,572 November 2003 Warrant Shares.
- ⁽¹²⁾ Includes 100,000 Deemed Outstanding Warrant Shares, 35,000 May 2004 Warrant Shares and 35,715 November 2003 Warrant Shares. Ramius Capital Group, LLC is the investment adviser to Portside Growth and Opportunity Fund and consequently has voting control and investment discretion over securities held by Portside. Ramius Capital disclaims beneficial ownership of the securities held by Portside. Peter A. Cohen, Morgan B. Stark, Thomas W. Strauss and Jeffrey M. Solomon are the sole managing members of C4S & Co., LLC, the sole managing member of Ramius Capital. As a result, Messrs. Cohen, Stark, Strauss and Solomon may be considered beneficial owners of securities deemed to be beneficially owned by Ramius Capital. Messrs. Cohen, Stark, Strauss and Solomon disclaim beneficial ownership of all of such securities.
- ⁽¹³⁾ Includes 83,333 Deemed Outstanding Warrant Shares.
- ⁽¹⁴⁾ Includes 32,667 Deemed Outstanding Warrant Shares.
- ⁽¹⁵⁾ Includes 100,000 Deemed Outstanding Warrant Shares.
- ⁽¹⁶⁾ Includes 116,667 Deemed Outstanding Warrant Shares. Highbridge Capital Management, LLC is the trading manager of Smithfield Fiduciary LLC and has voting control and investment discretion over securities held by Smithfield Fiduciary LLC. Glen Dubin and Henry Swieca control Highbridge Capital Management, LLC. Each of Highbridge Capital Management, LLC, Glen Dubin and Henry Swieca disclaims beneficial ownership of the securities held by Smithfield Fiduciary LLC.
- ⁽¹⁷⁾ Includes 83,333 Deemed Outstanding Warrant Shares.
- ⁽¹⁸⁾ Includes 150,000 Deemed Outstanding Warrant Shares and 27,777 May 2004 Warrant Shares.
- ⁽¹⁹⁾ Includes 50,000 Deemed Outstanding Warrant Shares and 21,429 November 2003 Warrant Shares.
- ⁽²⁰⁾ Includes 133,334 Deemed Outstanding Warrant Shares, 35,000 May 2004 Warrant Shares and 35,715 November 2003 Warrant Shares.
- ⁽²¹⁾ Includes 100,000 Deemed Outstanding Warrant Shares, 61,806 May 2004 Warrant Shares and 65,729 November 2003 Warrant Shares. Rodman & Renshaw LLC is a registered broker-dealer and NASD member.
- ⁽²²⁾ Assumes solely for purposes of this table that such shares are still owned upon completion of the offering; such assumption is not intended to override the Selling Stockholder table in, as applicable, the prospectus covering the November 2003 Warrant Shares or the prospectus covering the May 2004 Warrant Shares disclosing that such shares are anticipated to be sold under the respective prospectus.
- * Less than 1%.

PLAN OF DISTRIBUTION

The selling stockholders and any of their pledgees, assignees and successors-in-interest may, from time to time, sell any or all of their shares of common stock on any 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. The selling stockholders 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 date of this prospectus;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares under Rule 144 under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the selling stockholders may arrange for other broker-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. The selling stockholders do not expect these commissions and discounts to exceed what is customary in the types of transactions involved.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act of 1933

[Table of Contents](#)

amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

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 agreement or understanding, directly or indirectly, with any person to distribute the common stock.

We are required to pay all fees and expenses 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.

LEGAL MATTERS

The validity of the shares of common stock being offered hereby has been passed upon for Pro-Pharmaceuticals, Inc. by Perkins Smith & Cohen 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, 2003, 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 facilities the SEC maintains at Room 1024, Judiciary Plaza, 450 Fifth Street, N.W., Washington, D.C. 20549. You may also obtain copies of such material by mail from the Public Reference Section of the SEC (450 Fifth Street, N.W., Washington, D.C. 20549) at prescribed rates. Please call the SEC at 1-800-SEC-0330 for further information about the operation of the public reference rooms. Our SEC filings are also available at the SEC’s website at www.sec.gov.

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.

[Table of Contents](#)

Our world wide 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 them, 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 filed with the SEC on March 30, 2004 for the year ended December 31, 2003;
- (2) Our Quarterly Report on Form 10-Q filed with the SEC on August 16, 2004 for the three months ended June 30, 2004;
- (3) Our Current Report on Form 8-K filed with the SEC on August 16, 2004;
- (4) Our Current Report on Form 8-K filed with the SEC on September 2, 2004;
- (5) 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
- (6) 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