# PRO PHARMACEUTICALS INC Form SB-2 December 05, 2001

Registration No. 333-\_\_\_\_

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

FORM SB-2

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

PRO-PHARMACEUTICALS, INC. (Name of Small Business Issuer in its Charter)

Nevada 8731 04-3562325 (State or other jurisdiction of incorporation or organization) (Primary Standard Industrial incorporation or organization) Classification Code Number) Identification No.)

189 Wells Avenue, Suite 200
Newton, Massachusetts 02459
(617) 559-0033
(Address and Telephone Number of
Principal Executive Offices)

David Platt, Ph.D.

President and Chief Executive Officer
Pro-Pharmaceuticals, Inc.
189 Wells Avenue, Suite 200
Newton, Massachusetts 02459
(617) 559-0033
(Name, Address and Telephone Number
of Agent for Service)

with copies to:

Jonathan C. Guest, Esq.
Perkins, Smith & Cohen, LLP
One Beacon Street
Boston, Massachusetts 02108
(617) 854-4000

Approximate date of commencement of proposed sale to the public: As soon as possible after this Registration Statement is declared effective.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box [X]

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering  $[\ ]$ 

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering [ ]

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering [ ]

If delivery of the prospectus is expected to be made pursuant to Rule 434, check the following box  $[\ ]$ 

#### CALCULATION OF REGISTRATION FEE

Title of Each Class of	Number of	Proposed Maximum	Proposed Maximum
Securities to be	Units/Shares to be	Offering Price per	Aggregate Offering
Registered	Registered (1)	Unit (2)	Price (3)
Common Stock,	2,650,462	\$3.50	\$9,276,617
\$.001 par value	2,030,402	<b>γ</b> 3.30	79,210,011

- (1) Total represents 1,428,572 shares of Common Stock to be offered by the Registrant and up to 1,221,890 already issued shares of the Common Stock of the Registrant to be offered by selling security holders of the Registrant. In the event of a stock split, stock dividend or similar transaction involving the Common Stock of the Registrant, in order to prevent dilution, the number of shares registered shall be automatically increased to cover additional shares in accordance with Rule 416(a) under the Securities Act.
- (2) Represents proposed maximum price per share of Common Stock to be offered by the Registrant.
- (3) Estimated solely for the purpose of calculating the registration fee in accordance with Rule  $457\,(o)$  under the Securities Act, based on proposed maximum offering price per share of Common Stock to be offered by the Registrant.

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The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until this Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

The information contained in this prospectus is not complete and may be changed. Neither Pro-Pharmaceuticals nor the selling security holders may sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED DECEMBER \_\_\_\_, 2001

PRO-PHARMACEUTICALS, INC.

2,650,462 Shares of Common Stock \$.001 par value

Of the 2,650,462 shares of Pro-Pharmaceuticals common stock offered by this prospectus, 1,428,572 shares are being sold by Pro-Pharmaceuticals on a "best efforts" basis. The other 1,221,890 shares may be offered and sold, from time to time, by the selling security holders identified in this prospectus. We will not receive any of the proceeds from the sale of shares by the selling security holders.

There is currently no market for our common stock. We anticipate that we will retain a market maker to apply for trading of our common stock on the Over-the-Counter Bulletin Board following effectiveness of this registration statement.

INVESTING IN OUR COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. SEE "RISK FACTORS" BEGINNING ON PAGE 2 TO READ ABOUT CERTAIN RISKS YOU SHOULD CONSIDER 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.

	Price to Public	Placement Fees	Proceed (1) Company	
Per Share	\$	\$	\$	\$
Total (3)	\$	\$	\$	\$

- (1) The 1,428,572 shares offered by Pro-Pharmaceuticals are being offered principally to selected institutional and accredited investors. We have retained Atlas Capital Services, LLC, to act, on a best efforts basis, as our placement agent in connection with the arrangement of this transaction. We have agreed, among other things, to pay Atlas Capital a fee, including issuance of warrants, in connection with the arrangement of this financing and to indemnify Atlas Capital against certain liabilities, including liabilities under the Securities Act of 1933. See "Plan of Distribution."
- (2) Before deducting expenses payable by Pro-Pharmaceuticals estimated at \$120,000. We will not receive any proceeds from the sale of shares by the selling security holders.
- (3) We cannot assure you that any of the shares of common stock offered by this prospectus will be sold. Since the offering is made on a best efforts basis, there is no firm commitment by Atlas Capital to purchase or sell any of the shares of common stock. There is no minimum number of shares of common stock required to be sold by us, and no arrangements have been made to escrow any proceeds of the offering. Therefore, we may sell less than all of the shares of common stock offered hereby, which may significantly reduce the amount of proceeds that we receive. We anticipate concluding our offering of common stock 60 days after the date of this prospectus.

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Stock prices for biopharmaceutical and biotechnology companies are volatile
Our stock is not listed on any exchange or quoted on Nasdaq
If our stock is a "penny stock," your ability to trade our shares
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Purchasers of stock may be subject to substantial dilution
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### PROSPECTUS SUMMARY

About This Prospectus

This prospectus is part of a registration statement we filed with the U.S. Securities and Exchange Commission. You should rely only on the information

provided in this prospectus. Neither we, Atlas Capital nor the selling security holders listed in this prospectus have authorized anyone to provide you with information different from that contained in this prospectus. Pro-Pharmaceuticals and the selling security holders are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of common stock. Applicable SEC rules may require us to update this prospectus in the future. This preliminary prospectus is subject to completion prior to this offering.

About Pro-Pharmaceuticals, Inc.

We are currently in the development stage and have not yet generated any operating revenues. Since the formation in July 2000 of our predecessor, Pro-Pharmaceuticals, Inc., a Massachusetts corporation, we have been engaged in research and development activities in connection with identifying and developing a technology that will reduce toxicity and improve the efficacy of currently-used drug therapies, including cancer chemotherapies, by combining the drugs with a number of carbohydrate compounds. Our preliminary studies have identified certain mannans, a group of polysaccharides, that could be utilized as a potential drug delivery system. Polysaccharides are molecules consisting of one or more types of sugars. In the case of mannans, the principal component is the sugar mannose, which is similar to glucose. We believe that a mannan having a suitable chemical structure and composition, when attached to or combined with the active agent of a chemotherapy drug, would increase cellular membrane fluidity and permeability, thereby assisting delivery of the drug. We are currently conducting preclinical animal experiments.

#### Corporate Information

We were incorporated as "DTR-Med Pharma Corp." under Nevada law in January 2001 for the purpose of acquiring all the outstanding stock of our predecessor, Pro-Pharmaceuticals, Inc., which was a Massachusetts corporation engaged in a business we desired to acquire. From our incorporation until just before the acquisition, we were a wholly-owned subsidiary of Developed Technology Resource, Inc., a Minnesota corporation whose common stock is publicly traded on the Over-the-Counter Bulletin Board. In exchange for 1,221,890 shares of our common stock, Developed Technology transferred to us contractual rights that are described below under "Business -- Business of Pro-Pharmaceuticals -- Cancer Detection Technology." As part of that process, Developed Technology distributed its holdings of our common stock to its shareholders of record as of May 7, 2001. In anticipation of the acquisition of the Massachusetts company, we changed our name to "Pro-Pharmaceuticals, Inc."

On May 15, 2001, we acquired all of the outstanding common stock of the Massachusetts corporation. We acquired these shares in exchange for 12,354,670 shares of our common stock. As a result, that corporation became our wholly owned subsidiary, and its shareholders through an exchange owned approximately 91% of the outstanding shares of our common stock, with the Developed Technology shareholders owning the remaining 9%. See "Security Ownership of Certain Beneficial Owners and Management" for information about the ownership of our common

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stock. After the acquisition, we merged with the Massachusetts corporation and are the surviving corporation in the merger.

As required by the stock exchange agreement that effected the acquisition,

we registered our common stock under the Securities Exchange Act of 1934 by filing a Registration Statement on Form 10-SB with the Securities and Exchange Commission that became effective on August 13, 2001. Our articles of organization provide that our common stock may not be sold without our approval until the 90th day after the date our common stock is registered. Accordingly, our common stock became eligible for transfer, subject to applicable federal and state securities law requirements, as of November 11, 2001. We anticipate that we will retain a market maker to apply for trading of our common stock on the Over-the-Counter Bulletin Board following effectiveness of this registration statement.

Our address is 189 Wells Avenue, Suite 200, Newton, Massachusetts 02459. Our telephone number is (617) 559-0033, fax number is (617) 928-3450, e-mail address is Plattpharma@aol.com, and our website address is www.pro-pharmaceuticals.com.

#### THE OFFERING

Common stock offered by us:

1,428,572 shares

Common stock offered by the selling security holders:

1,221,890 shares

Common stock currently outstanding before the offering (as of November 21, 2001):

15,148,146 shares

Common stock to be outstanding after the

16,576,718 shares

offering assuming sale of all common stock offered by us:

Use of Proceeds:

We intend to use the net proceeds of this offering to fund research and development activities, conduct pre-clinical experiments, and for other general corporate purposes.

We will not receive proceeds from the sale of shares by the selling security holders.

#### 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 the major factors under the heading "Risk 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, no market may develop for our common stock or, if there

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is a market, the trading price of our common stock could decline, and you could lose part or all of your investment.

We are at an early stage of development without operating history.

We are a development-stage venture without operating history. Our future revenues and profits are uncertain. We were incorporated in January 2001. Our predecessor, Pro-Pharmaceuticals (Massachusetts) was incorporated in July 2000. We have not generated any revenues to date. Though we have prepared and tested several carbohydrate-based formulations in preclinical studies, we have not prepared formulations of any therapeutic product for testing, and we have not commenced any clinical trials. We have no therapeutic products available for sale, and none are expected to be commercially available for several years, if at all. Our research activities may not lead to the development of any commercially viable products. We may never generate revenue or become profitable, even if we are able to commercialize any products. If we are unable to generate revenues or profits, you might not be able to realize returns on your investment in our company. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

We have incurred net losses to date and depend on outside capital.

Our predecessor, Pro-Pharmaceuticals (Massachusetts) had incurred net operating losses since its incorporation in July 2000. Our accumulated deficit as of September 30, 2001 was approximately \$1,626,872. We will need to conduct significant research, development, testing and regulatory compliance activities that, together with projected general and administrative expenses, we expect will result in substantial increasing operating losses for at least the next several years. Accordingly, we will not be generating our own capital and will remain dependent on outside sources of financing during that time.

As of September 30, 2001, we had approximately \$865,913 in cash and cash equivalents. We have budgeted expenditures for the twelve-month period ending December 31, 2002 of \$4,500,000. We attempted to fund these expenditures through proceeds of a private placement that we began in May 2001. We abandoned the private placement as of December 3, 2001, and terminated all offering activity on or before that date. We raised \$2,237,500 prior to termination.

We will require substantial funds to: (1) continue our research and development programs, (2) acquire technologies by license or purchase, and (3) conduct preclinical studies and clinical trials. We may need to raise additional capital to fund our operations repeatedly. We may raise such capital through public or private equity financings, partnerships, debt financings, bank borrowings, or other sources. Our capital requirements will depend upon numerous factors, including the following:

- o the establishment of collaborations
- o the development of competing technologies or products
- o changing market conditions
- o the cost of protecting our intellectual property rights
- o the progress of our research and development programs, the progress of our collaborations and receipt of any option/license, milestone and royalty payments resulting from those collaborations

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#### o technology acquisition opportunities

Additional funding may not be available on 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, you may experience dilution of your proportionate ownership of the company.

We may not be able to sell all of the shares we are currently offering.

Upon this registration becoming effective, we plan to offer and sell to institutional and accredited investors identified by Atlas Capital Services, LLC, as our placement agent, shares of our common stock for proceeds of up to \$5,000,000 before expenses. Please see "Plan of Operation -- Liquidity and Capital Resources" for further discussion of our present financing plans. If we sell all of the 1,428,572 shares through Atlas Capital that we are offering by this prospectus, our estimated proceeds would be \$4,455,000 after deducting the estimated placement fee of \$425,000 and offering expenses including \$20,000 as a placement agent due diligence fee and estimated \$100,000 for accounting, legal and printing expenses. We cannot assure you that we will succeed in selling any or all of the shares of common stock we are currently offering. We have not fixed a minimum number of shares of common stock to be sold by us in this offering. Therefore, we may sell less than all of the shares of common stock offered by this prospectus, which may significantly reduce the amount of proceeds we receive. In any case, we will have to raise additional funds to continue the development of our technologies and complete the commercialization of products, if any, resulting from our technologies.

Our product candidates will be based on novel technologies.

Our product candidates will be based upon novel technologies that we plan to use to apply to drugs currently used in the treatment of cancer and other diseases. These technologies have not been proven. 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. Furthermore, as is often the case, preclinical results in animal studies may not predict outcomes in human clinical trials. Our product candidates may not be proven safe or effective. If this technology does not work, our product candidates may not develop into commercial products.

We must successfully develop products in order to generate revenue.

Our product candidates are still in research and preclinical development, which means that they have not yet been tested on humans. We will need to commit significant time and resources to develop these and additional product candidates. We are dependent on the successful completion of clinical trials and obtaining regulatory approval in order to generate revenues. The failure to generate such revenues may preclude us from continuing our research and development of these and other product candidates.

We have no product candidates in clinical trials, and we do not know when, if ever, we will have a candidate and commence 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 in three phases (phases I, II, and III) 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. A number

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of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials, even after reporting promising results in earlier trials. In addition, data obtained from clinical trials are susceptible to varying interpretations. Government regulators and our collaborators may not agree with our interpretation of our future clinical trial results. The clinical trials of any of our future product candidates may not be successful.

We will need regulatory approvals to commercialize our products.

We do not have any product approved for sale in the U.S. or any foreign market. We must 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 drug products in other countries. We have not yet submitted any application for approval to the FDA. Once an application is submitted, the FDA could reject the 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.

The regulatory review and approval process is lengthy, expensive and uncertain. Extensive preclinical 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. We have no experience in obtaining such approvals, and cannot be certain when we will receive these regulatory approvals, if ever.

In addition to initial regulatory approval, our product candidates will be subject to extensive and rigorous ongoing domestic and foreign government regulation, as we discuss in more detail in "Business -- Business of Pro-Pharmaceuticals -- Government Regulation," below. Any approvals, once obtained, may be withdrawn if compliance with regulatory requirements is not maintained or safety problems are identified. Failure to comply with these requirements may subject us to stringent penalties.

Our product candidates may not be successfully commercialized.

Even if our product candidates are successful in clinical trials, they may not be successfully commercialized. All of our compounds currently are in research or development, and none has been submitted for marketing approval. There can be no assurance that any of our compounds will enter human clinical trials on a timely basis, if at all, or that we will develop any product candidates suitable for commercialization. Prior to commercialization, each product candidate will require significant additional research, development and preclinical testing and extensive clinical investigation before submission of any regulatory application for marketing approval. Potential products that appear to be promising at early stages of development may not reach the market for a number of reasons. Potential products may:

- o be found ineffective or cause harmful side effects during preclinical testing or clinical trials
- o fail to receive necessary regulatory approvals
- o be difficult to manufacture on a large scale

- o be uneconomical to produce
- o fail to achieve market acceptance
- o be precluded from commercialization by proprietary rights of third parties

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We cannot assure you that we will undertake any product development efforts, either alone or with collaborative partners. If we do undertake product development efforts, we cannot assure you that any of those efforts will be successfully completed, that required regulatory approvals will be obtained or that any products, if introduced, will be successfully marketed or achieve customer acceptance.

We have no experience in clinical trials.

We have no experience in conducting clinical trials and will be dependent on others to conduct our clinical trials. We intend to rely on academic institutions or clinical research organizations to conduct, supervise or monitor some or all aspects of clinical trials involving our products. In addition, certain clinical trials for our products may be conducted by government-sponsored agencies and consequently will be dependent on governmental participation and funding. We will have less control over the timing and other aspects of these clinical trials than if we conducted them entirely on our own. We cannot assure you that these trials will commence or be completed as we expect or that they will be conducted successfully. Failure to commence or complete, or delays in, any of our planned clinical trials could delay or prevent the commercialization of our products and harm our business. The actual timing of clinical trials can vary dramatically due to factors such as delays, scheduling conflicts with participating clinicians and clinical institutions and the rate of patient accruals. We cannot assure you that clinical trials involving our product candidates will commence or be completed as forecasted.

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:

- o obtain patent protection for our products or processes both in the United States and other countries
- o protect trade secrets
- o prevent others from infringing on our proprietary rights

While we believe that linking our carbohydrate polymers to existing drugs will yield patentable subject matter, to date we have only two pending patent applications, as well as a provisional patent application as discussed below under "Business -- Business of Pro-Pharmaceuticals -- Patents and Proprietary Rights." We do not believe that our carbohydrate-drug conjugates will infringe any third-party patents covering the underlying drug. However, there can be no assurance that we will receive a patent for our carbohydrate-drug conjugates. In addition, we must meet further filing deadlines in the case of our provisional patent applications if we are to retain the filing, or priority, dates for those applications, as discussed below under "Business -- Business of

Pro-Pharmaceuticals -- Patents and Proprietary Rights."

Since patent applications in the United States are maintained in secrecy until patents are issued, and since publication of discoveries in the scientific or patent literature often lag behind actual discoveries, we cannot be certain that we are the first to make the inventions to be covered by the patent applications we intend to file. 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. If it allows broad claims, the number and cost of patent interference

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proceedings in the U.S. and the risk of infringement litigation may increase. If it allows narrow claims, the risk of infringement may decrease, but the value of our rights under our patents, licenses and patent applications may also decrease.

We cannot assure you that patent applications in which we have rights will ever 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. Litigation, interference proceedings or other governmental proceedings that we may become involved in with respect to our proprietary technologies or the proprietary technology of others could result in substantial cost to us. Patent litigation is widespread in the biotechnology industry, and any patent litigation could harm our business. Costly 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. An adverse outcome in litigation with respect to the validity of any of our patents could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to cease using a product or technology.

We also rely upon trade secrets, proprietary know-how and continuing technological innovation to remain competitive. Third parties may independently develop such know-how or otherwise obtain access to our technology. While our employees, consultants and corporate partners with access to proprietary information generally will be required to enter into confidentiality agreements, these agreements may not be honored.

Patents issued to third parties may cover our products as ultimately developed. We may need to acquire licenses to these patents or challenge the validity of these patents. We may not be able to license any patent rights on acceptable terms or successfully challenge such patents. The need to do so will depend on the scope and validity of these patents and ultimately on the final design or formulation of the products and services that we develop. We may not be able to meet our obligations under those licenses that we do enter into. If we enter into a license agreement for intellectual property underlying any of our products, and that license were to be terminated, we may lose our right to market and sell any products based on the licensed technology.

Our products could infringe on the intellectual property rights of others.

Although we attempt to monitor the patent filings of our competitors in an effort to guide the design and development of our products to avoid infringement, third parties may challenge the patents that have been issued or licensed to us. We may have to pay substantial damages, possibly including

treble damages, for past infringement if it is ultimately determined that our products infringe a third party's patents. Further, we may be prohibited from selling our products before we obtain a license, which, if available at all, may require us to pay substantial royalties. Even if infringement claims against us are without merit, defending a lawsuit takes significant time, may be expensive and may divert management attention from other business concerns.

Our lack of operating experience may cause us difficulty in managing our growth.

We have no experience in manufacturing or procuring products in commercial quantities and conducting other later-stage phases of the regulatory approval process, or in selling pharmaceutical products, and we have only limited experience in negotiating, establishing and maintaining strategic relationships. We have no experience with respect to the launch of a commercial product. Our ability to manage our growth, if any, will require us to improve and expand our management and our operational and financial systems and controls. If our management is unable to manage growth effectively, our business and financial condition would be

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materially harmed. In addition, if rapid growth occurs, it may strain our operational, managerial and financial resources.

Our business is subject to technological obsolescence.

Biotechnology and related pharmaceutical technology have undergone and are subject to rapid and significant change. We expect that the technologies associated with biotechnology research and development will continue to develop rapidly. Our future will depend in large part on our ability to maintain a competitive position with respect to these technologies. Any compounds, products or processes that we develop may become obsolete before we recover any expenses incurred in connection with developing these products.

We face intense competition in the biotechnology and pharmaceutical industries.

The biotechnology and pharmaceutical industries are intensely competitive. We have numerous competitors in the United States and elsewhere. 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 have become increasingly aware of the commercial value of their research findings. These institutions are now more likely to enter into exclusive licensing agreements with commercial enterprises, including our competitors, to market commercial products. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical and established biotechnology companies. Many of these competitors have significant products that have been approved or are in development and operate large, well-funded research and development programs.

Our competitors may succeed in developing or licensing technologies and products that are more effective or less costly than any we are developing. Our competitors may succeed in obtaining FDA or other regulatory approvals for product candidates before we do. In particular, we face direct competition from many companies focusing on delivery technologies. Products resulting from our research and development efforts, if approved for sale, may not compete successfully with our competitors' existing products or products under development.

We will depend on third parties to manufacture and market our products.

We do not have, and do not intend to develop, internal facilities for the manufacture of any of our products for clinical or commercial production. We will need to develop relationships with third-party manufacturing resources, enter into collaborative arrangements with licensees or other parties which have established manufacturing capabilities or elect to have other third parties manufacture our products on a contract basis. We expect to be dependent on such collaborators or third parties to supply us in a timely way with products manufactured in compliance with standards imposed by the FDA and foreign regulators. The manufacturing facilities of contract manufacturers may not comply with applicable manufacturing regulations of the FDA nor meet our requirements for quality, quantity or timeliness.

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 pharmaceutical products. If we develop products eligible for commercial sale, we will need to rely on third parties such as licensees, collaborators, joint venture partners or independent distributors to market and sell those products. We may not be able to obtain access to a marketing and sales force with sufficient technical expertise and distribution capability. Also, we will not be able to control the resources and

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effort that a third party will devote to marketing our products. If we are unable to develop and maintain relationships for the necessary marketing and sales capabilities, we may fail to gain market acceptance for our products, and our revenues could be impaired.

We depend on key personnel to develop our products and pursue collaborations.

We are highly dependent on Dr. David Platt, President and Chief Executive Officer, and Dr. Anatole Klyosov. Dr. Klyosov is a member of our Scientific Advisory Board and he owns 50% of MIR International, Inc., which provides consulting services regarding our research and development. The loss of either 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 not entered into an employment agreement with Dr. Platt. Neither Dr. Platt nor Dr. Klyosov has entered into an assignment of inventions or confidentiality agreement with us.

Recruiting and retaining qualified scientific personnel to perform research and development work are critical to our success. There is intense competition for qualified scientists and managerial personnel from numerous pharmaceutical and biotechnology companies, as well as from academic and government organizations, research institutions and other entities. In addition, we may face particular difficulties because there is a limited number of scientists specializing in carbohydrate chemistry, a principal focus of our company. We expect to rely on consultants and advisors, including our scientific and clinical advisors, to assist us in formulating our research and development strategy. Any of those consultants or advisors could be employed by other employers, or be self-employed, and might have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. Such other employment, consulting or advisory relationships could place our trade secrets at risk, even if we require non-disclosure agreements.

A former employer of our President alleged violation of his noncompetition agreement.

SafeScience, Inc. (now known as GlycoGenesys, Inc.), former employer of Dr. David Platt, our President and Chief Executive Officer, alleged in a letter dated February 15, 2001, that his engagement with our business is a violation of a noncompetition covenant he has with SafeScience. In a letter dated February 19, 2001, Dr. Platt responded, stating that our business is not competitive because, among other things, we are developing methods to reduce toxicity of currently existing chemotherapy drugs, whereas SafeScience is engaged in new drug development. Counsel for SafeScience indicated a willingness to resolve these matters but attempts to set up a meeting were unsuccessful. We cannot assure you that Safe Science will not proceed to take further action.

We face potential difficulties in obtaining product liability and related insurance.

We do not have product liability or other professional liability insurance. In the future, we may, in the ordinary course of business, be subject to substantial 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. We do not currently have any product liability or professional liability insurance, and it is possible that we will not be able to obtain or maintain such insurance on acceptable terms or that any insurance obtained will provide adequate coverage against potential liabilities. Our inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or limit the commercialization of any products we develop. A successful product liability claim in excess of our insurance coverage could exceed our net worth. While we desire to reduce our risk by obtaining indemnity undertakings with respect to such claims

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from licensees and distributors of our products, we may not be able to obtain such undertakings and, even if we do, they may not be sufficient to limit our exposure to claims.

Health care cost containment initiatives 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 or reduce the cost of health care. Governmental and other third-party payors increasingly are attempting to contain health care costs by:

- o challenging the prices charged for health care products and services
- o limiting both coverage and the amount of reimbursement for new therapeutic products
- o denying or limiting coverage for products that are approved by the FDA but are considered experimental or investigational by third-party payors
- o refusing in some cases to provide coverage when an approved product is used for disease indications in a way that has not received FDA marketing approval

In addition, the trend toward managed health care in the United States, the

growth of organizations such as health maintenance organizations, and legislative proposals to reform healthcare and government insurance programs could significantly influence the purchase of healthcare services and products, resulting in lower prices and reducing demand for our products.

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. While we cannot predict whether any such legislative or regulatory proposals will be adopted, the adoption of such proposals could make it difficult or impossible to sell our products.

Environmental regulations may affect our manufacturers and other contractors.

Pharmaceutical research and development involves the controlled use of hazardous materials including but not limited to certain hazardous chemicals and radioactive materials. In connection with research, development and manufacturing activities, biotechnology and biopharmaceutical companies are subject to federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials, biological specimens and wastes. Since we do not anticipate building in-house research, development or manufacturing facilities, but plan to have these activities conducted by contractors and other third parties, we do not anticipate that we will be directly affected by environmental regulations. However, our contractors and others conducting research, development or manufacturing activities for us may be required to incur significant costs to comply with environmental and health and safety regulations in the future, and this could in turn affect our costs of doing business and might ultimately interfere with timely completion of research or manufacturing programs if those third parties are unable to comply with environmental regulatory requirements.

Our ability to conduct animal testing could be limited in the future.

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Our research and development activities have involved, and will continue to involve, animal testing. Such activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas. To the extent the activities of these groups are successful, our business could be materially harmed.

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.

Factors that may have a significant impact on the market price and marketability of our common stock include:

o announcements of technological innovations or new commercial

therapeutic products by us, our collaborative partners or our present or potential competitors

- o announcements by us or others of results of preclinical testing and clinical trials
- o developments or disputes concerning patent or other proprietary rights
- o adverse legislation, including changes in governmental regulation and the status of our regulatory approvals or applications
- o changes in health care policies and practices
- o economic and other external factors, including general market conditions

In the past, following periods of volatility in the market price of a company's securities, securities class action litigation has often been instituted. If a securities class action suit is filed against us, we would incur substantial legal fees and our management's attention and resources would be diverted from operating our business in order to respond to the litigation.

Our stock is not listed on any exchange or quoted on Nasdaq.

We have not listed our capital stock on any exchange and do not foresee that in the near-term we would be able to meet the listing standards for any exchange or for the Nasdaq National Market or the Nasdaq SmallCap Market. We are contemplating taking, but have not yet taken any, steps to permit our shares to be traded over the counter including on the over-the-counter bulletin board (OTCBB) sponsored by the National Association of Securities Dealers. There may be, but we cannot assure, a market for our shares on the OTCBB. Accordingly, our stockholders may not find a market for their shares and be unable to sell their shares when they want or at a favorable price.

If our stock is a "penny stock," your ability to trade our shares could be adversely affected.

The SEC has adopted regulations imposing limitations upon the manner in which certain low priced equity securities, referred to as "penny stocks," are publicly traded. Under these regulations, a penny stock is defined as any equity security that has a market price of less than

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\$5.00 per share, subject to certain exceptions. These exceptions include any equity security listed on a national exchange, the Nasdaq National Market System or SmallCap Market and any equity security issued by a company meeting specified requirements for net tangible assets or revenues. Unless an exception is available, the regulations require the delivery, prior to any transaction involving a penny stock, of a disclosure schedule explaining the penny stock market and the associated risks. The regulations also require certain broker-dealers who recommend penny stocks to persons other than established customers and certain accredited investors to make a special written suitability determination for the purchaser and receive the purchaser's written agreement to a transaction prior to sale. These requirements make it more difficult to effect transactions in penny stocks as compared to other securities.

Our common stock is not yet publicly traded. Since we do not meet any of the requirements that would exempt us from the \$5.00 per share market price requirement, our stock must trade above that level in order for it not to be

classified as a "penny stock." We are uncertain that trading prices at this level can be established or sustained. Should trading prices fall below \$5.00 per share, our shares could be considered a "penny stock" and your ability to trade our shares could accordingly be adversely affected.

Purchasers of stock may be subject to substantial dilution.

We are offering our common stock to the public at a price that is substantially higher than the net tangible book value per share of our common stock, as discussed in "Dilution," below. If you purchase common stock that Pro-Pharmaceuticals is offering with this prospectus, you will therefore incur immediate and substantial dilution.

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 82% of our outstanding shares of our common stock, and Dr. Platt and Mr. Czirr together own approximately 65%. Even if we sell all of the 1,428,572 shares that we are currently offering in this prospectus, the four stockholders named above would still control approximately 75% of our common stock, with Dr. Platt and Mr. Czirr together controlling about 60%. Some or all of these stockholders, acting in concert, will be able to continue to elect the Board of Directors and take other corporate actions requiring stockholder approval, such as recapitalization or other fundamental corporate action, as well as dictate 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.

#### FORWARD-LOOKING STATEMENTS

This prospectus contains "forward-looking" statements that involve risks and uncertainties. Forward-looking statements include statements about the desired or believed utility and market for our potential products, future of the biotechnology and biopharmaceutical industry, statements about future business plans and strategies, and most other statements that are not historical in nature. Because forward-looking statements involve risks and uncertainties, there are factors, including those discussed below, that could cause actual results to be materially different from any future results, performance or achievements expressed or implied. Accordingly, 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.

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#### USE OF PROCEEDS

If we sell all of the 1,428,572 shares we are offering by this prospectus through Atlas Capital, our estimated proceeds would be \$4,455,000 after deducting the estimated placement fee and offering expenses. We cannot assure you that we will succeed in selling any or all of the shares of common stock we are currently offering. See "Risk Factors -- We may not be able to sell all of the shares we are currently offering" for further discussion about risks connected with this offering.

We will not receive any proceeds from the sale of common stock by the selling security holders.

We expect to use approximately \$3,200,000 of the aggregate net proceeds of this offering to fund our research and development efforts, including ongoing development of our technologies, pre-clinical and clinical testing and other costs associated with our pharmaceutical discovery and development programs. The remainder of the aggregate net proceeds will be used for working capital and general corporate purposes including general and administrative (\$1,000,000), equipment and leaseholds (\$100,000) and contingency allowance (\$150,000).

The amounts actually expended for each purpose may vary significantly depending upon a number of factors, including:

- o the progress of our drug delivery research and development efforts
- o our ability to establish collaborative arrangements
- o progress with pre-clinical studies and clinical trials
- o the time and costs involved in obtaining regulatory approvals
- o the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims
- o competing technological and market developments
- o changes in our collaborative relationships, if any
- o costs associated with the acquisition of technology, if any
- o evaluation of the commercial viability of potential products

Based on current projections, we estimate that our existing capital resources, together with the net proceeds from this offering, will be sufficient to fund our requirements for approximately twelve months. Pending such uses, we intend to invest the aggregate net proceeds from this offering in short-term, investment-grade, interest-bearing securities. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to ours, although no agreements have been entered into as of the date of this prospectus with respect to any such acquisition or investment. See "Plan of Operation," below, for further discussion of our operating plans.

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#### MARKET FOR OUR COMMON STOCK AND RELATED STOCKHOLDER MATTERS

Market for Our Common Stock

There is currently no market for our common stock. We anticipate that we will retain a market maker to apply for trading of our common stock on the Over-the-Counter Bulletin Board following effectiveness of this registration statement. Our articles of organization provide that our common stock may not be sold without our approval until the 90th day after the date our common stock is registered under the Securities Exchange Act of 1934. We registered our common stock under the Exchange Act by filing a Registration Statement on Form 10-SB, which became effective as of August 13, 2001. Accordingly, our common stock became eligible for transfer, subject to applicable federal and state securities law requirements, as of November 11, 2001.

Shares Subject to Future Issuance

Convertible Notes

As of November 15, 2001, we had outstanding \$195,000 principal amount of notes which are convertible into 97,500 shares of our common stock at a conversion price of \$2.00 per share. The \$195,000 principal amount represents the notes that are outstanding following an early conversion offer we made to noteholders as described below under "Plan of Operation -- Liquidity and Capital Resources."

Common Stock Warrants

Private Placement (terminated)

We began in May 2001 a private placement of securities consisting of 1,470,000 units, offered at \$3.50 each, of one share of our common stock and one warrant to purchase one share of our common stock. Such purchases will result in our issuing 689,300 shares of our common stock and warrants to purchase 689,300 shares of our common stock. We granted one purchaser of a large block of units an option to purchase an additional 200,000 units on the same terms as that investor's current purchase. For detail about this private placement, see "Plan of Operation -- Liquidity and Capital Resources" below. We abandoned the private placement as of December 3, 2001, and terminated all offering activity on or before that date.

Warrants Issued to Former Holders of Convertible Notes

In response to our offer for early conversion of our convertible notes, holders of an aggregate of \$1,115,602 of principal amount of the convertible notes have requested conversion of their notes. This will result in issuance of an additional 557,801 common stock purchase warrants identical to the warrants being offered in our terminated private placement.

Stock Incentive Plan

On October 18, 2001, our Board of Directors adopted the "Pro-Pharmaceuticals, Inc. 2001 Stock Incentive Plan" which permits awards of incentive and non-qualified stock options and other forms of incentive compensation to employees and nonemployees such as directors and consultants. The Board reserved 2,000,000 of our shares of common stock for awards pursuant to the plan, all of which reserved shares could be awarded as incentive stock options. The Board agreed to recommend the plan to our stockholders for approval at the next annual or special meeting

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of stockholders. As of November 26, 2001, we have granted Burton Firtel, a director of our company, a non-qualified stock option under the plan to purchase 200,000 shares of common stock. The option is immediately exercisable as to 120,000 shares. See "Management -- Compensation of Directors and Advisors" for further information about this option grant.

Shares Eliqible for Sale Pursuant to Rule 144 under the Securities Act

As of November 21, 2001, 15,148,146 shares of our common stock are outstanding, including 1,221,890 shares which were issued as a dividend to the stockholders of Developed Technology Resource, Inc., and 12,354,670 shares which were issued to the former shareholders of Pro-Pharmaceuticals (Massachusetts). All of our outstanding shares, except for the 1,221,890 shares issued as a dividend to the Developed Technology stockholders, are restricted securities within the meaning of Rule 144 under the Securities Act of 1933 and may not be sold in the absence of registration under the Securities Act unless an exemption

from registration is available, including an exemption contained in Rule 144 under the Securities  $\mbox{Act.}$ 

In general, under Rule 144 as currently in effect, a person (or persons whose shares are aggregated), including an affiliate, as that term is defined in Rule 144 under the Securities Act, who has beneficially owned shares for at least one year is entitled to sell, within any three-month period, a number of such shares that does not exceed the greater of (1) one percent of the then outstanding shares of common stock (approximately 151,481 shares as of November 21, 2001) or (2) the average weekly trading volume in the common stock in the Over-the-Counter market during the four calendar weeks preceding the date on which notice of such sale is filed, provided certain requirements concerning availability of public information, manner of sale and notice of sale are satisfied. In addition, our affiliates must comply with the restrictions and requirements of Rule 144, other than the one-year holding period requirement, in order to sell shares of common stock which are not restricted securities.

Under Rule 144(k), a person who is not an affiliate and has not been an affiliate for at least three months prior to the sale and who has beneficially owned shares for at least two years may resell such shares without compliance with the foregoing requirements. In meeting the one- and two-year holding periods described above, a holder of shares can include the holding periods of a prior owner who was not an affiliate. The one- and two-year holding periods described above do not begin to run until the full purchase price or other consideration is paid by the person acquiring the shares from the issuer or an affiliate.

The 12,354,670 shares of our common stock issued to the shareholders of Pro-Pharmaceuticals (Massachusetts) in exchange for their Pro-Pharmaceuticals (Massachusetts) common stock will become eligible for sale pursuant to Rule 144 under the Securities Act on May 15, 2002, which is one year from the date of the exchange. We have no agreements with any holder of our common stock or warrants that would require us to register any common stock under the Securities Act for sale by security holders.

#### Holders

As of November 21, 2001, there were 180 holders of record of our common stock, although we believe that there are additional beneficial owners of our common stock who own their shares in "street name."

### Dividends

There have been no cash dividends declared on our common stock since our company was formed. Dividends are declared at the sole discretion of our Board of Directors.

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### PLAN OF OPERATION

This Plan of Operation and other parts of this prospectus contain forward-looking statements that involve risks and uncertainties. All forward-looking statements included in this document are based on information available to us on the date hereof, and we assume no obligation to update any such forward-looking statements. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of a number of factors, including those set forth in "Risk Factors" and elsewhere in this prospectus.

Liquidity and Capital Resources

We were incorporated in January 2001 for the purpose of effecting a business combination with Pro-Pharmaceuticals, Inc., a Massachusetts corporation. The transaction included a merger in which we are the surviving corporation. The business combination has been accounted for using purchase accounting, with the assets and liabilities of the acquired company being recorded at fair value. The merger and related transactions are discussed below under "Business -- Initial Corporate Organization, Acquisition and Merger."

Our capital resources to date consist of (i) the proceeds of a private placement of convertible notes issued and sold by the predecessor Massachusetts company in anticipation of its being acquired by us and (ii) the proceeds of a private placement begun in May 2001 of our common stock and stock purchase warrants. Each is further described below.

Commencing in December 2000 and continuing through May 2001, Pro-Pharmaceuticals (Massachusetts) issued convertible notes with an aggregate principal amount of \$1,310,602 to "accredited investors" as such term is defined in Regulation D promulgated under the Securities Act of 1933. These notes are now our corporate obligations as a result of the merger with Pro-Pharmaceuticals (Massachusetts). The notes have an interest rate of 10% per year and mature one year from their issuance dates. The notes are convertible into shares of our common stock, at a conversion price of \$2.00 per share. Pursuant to our early conversion offer, described below, holders of an aggregate of \$1,115,602 of principal amount of the convertible notes have requested conversion of their notes.

We began as of May 25, 2001 a private placement of securities exempt from registration pursuant to Rule 506 of Regulation D under the Securities Act of 1933 in order to raise \$5,145,000 to cover our expenditures. We abandoned this private placement as of December 3, 2001, and terminated all offering activity on or before that date. Purchasers under the private placement had to qualify as "accredited investors" as such term is defined in Regulation D. The offered securities comprised up to 1,470,000 units, offered at \$3.50 each, of one share of our common stock and one 4-year warrant exercisable at \$6.50 to purchase one share of our common stock. We sold 689,300 units as of the date we abandoned the offering. The warrant is subject, following written notice, to acceleration if either (i) we file a New Drug Application with the FDA, or (ii) our stock is listed on an exchange and its closing price exceeds \$11.00 on any 10 trading days within a period of 20 consecutive trading days or, if our stock is quoted on the NASDAQ National Market System or Small Cap Market, or over-the-counter, and the average of the closing bid and asked prices thereon exceeds \$11.00 on any 10 trading days within a period of 20 consecutive trading days.

In connection with agreements with three investors in this offering who were each willing to invest a substantial amount of funds, we sold units at \$3.00 each, as follows: 133,400 of the units for a total of \$400,200; 66,700 units for a total of \$200,100; and 150,000 units for a total of

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\$450,000. We reduced each investor's warrant exercise price to \$5.00, and changed the warrant acceleration provision to lower the 10-day closing price threshold to \$10.00. We also granted the earliest of these investors an option to purchase an additional 200,000 units on the same terms as that investor's current purchase. The option is exercisable at any time until 30 days after we notify the investor of our receipt of notice that an investigational new drug application filed by us with the FDA has become effective for any one of our compounds. As a result of agreeing to accept different terms on the offered

securities with these investors, we are notifying each previous purchaser of the sale to those investors. This could result in our agreeing to refund some or all of the previous investments.

As of the termination of this private placement in December 2001, we had received proceeds of \$2,237,500 from the sale of the securities offered in this private placement. Such purchases will result in our issuing 689,300 shares of our common stock and warrants to purchase 689,300 shares of our common stock.

We have requested that the holders of the convertible notes described above convert them, in accordance with their terms, to shares of our common stock prior to the notes' maturity dates. In order to encourage early conversion by September 7, 2001, we offered to issue each noteholder who converts a common stock purchase warrant identical to the warrant offered in our terminated private placement. In the case of a noteholder who accepted our offer, the warrant we issue is exercisable to purchase such number of shares as is equal to the number of shares of our common stock that the holder receives as of the conversion of the note. In response to our offer, holders of an aggregate of \$1,115,602 of principal amount of the convertible notes have requested conversion of their notes.

Regardless of whether a noteholder accepted our early conversion offer or later decides to convert each of our noteholders is entitled to receive, as "additional consideration" for originally purchasing the note, one-half (1/2) share of our common stock for each dollar of principal. We are completing our issuance an aggregate of 655,301 of such "additional compensation" shares. Based upon the offering price of the securities in our private placement, the conversion price under the convertible note is now fixed at one share of our common stock for each two dollars (\$2.00) of unpaid principal and interest. All shares of common stock issued upon conversion of the notes are "restricted securities" as defined in Rule 144 under the Securities Act.

As of September 30, 2001, we had approximately \$865,913, and as of October 31, 2001 approximately \$852,092, in cash and cash equivalents. We have budgeted expenditures for the twelve-month period ending December 31, 2002, of \$4,500,000, comprised of anticipated expenditures for research and development (\$3,200,000), general and administrative (\$1,000,000), equipment and leaseholds (\$100,000) and contingency allowance (\$150,000).

Additional funds may be raised through additional equity financings, as well as borrowings and other resources. With the capital we have raised to date, and the additional \$5,000,000 under the offering described in this prospectus that we are attempting to raise, we believe that we will be able to proceed with our current plan of operations and meet our obligations for approximately the next twelve months. If we do not raise the additional funds, we will have to cut our research and development expenditures to a minimum level for the next twelve months, since available cash at October 31, 2001 would be insufficient to cover more than equipment and leasehold costs and some administrative costs. In that case, overall administrative expenses for the next twelve months would have to be cut by approximately \$500,000. If we have only minimal funds to spend on research and development, that would substantially slow progress that we might expect to make during the next twelve months in development of our business including commencement of clinical trials.

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We expect to generate losses from operations for several years due to substantial additional research and development costs, including costs related to clinical trials. Our future capital requirements will depend on many factors, in particular our progress in and scope of our research and development

activities, and the extent to which we are able to enter into collaborative efforts for research and development and, later, manufacturing and marketing products. We may need additional capital to the extent we acquire or invest in businesses, products and technologies. If we should require additional financing due to unanticipated developments, additional financing may not be available when needed or, if available, we may not be able to obtain this financing on terms favorable to us or to our stockholders. Insufficient funds may require us to delay, scale back or eliminate some or all of our research and development programs, or may adversely affect our ability to operate as a going concern. If additional funds are raised by issuing equity securities, substantial dilution to existing stockholders may result.

#### CAPITALIZATION

The following table sets forth our capitalization as of September 30, 2001, and also our capitalization as adjusted to reflect the sale of 1,428,572 shares of our common stock that we are offering with this prospectus, at an assumed maximum public offering price of \$3.50 per share, and receipt of net proceeds from this sale of \$4,455,000. See "Use of Proceeds" for further information about our anticipated proceeds to us from this offering.

	September 30, 2001	
	Actual	As Adjusted
Common voting shares, \$0.001 par value, 100,000,000 shares authorized and 14,727,226		
shares outstanding actual and 16,155,798 shares outstanding pro forma as adjusted (1) Undesignated shares, \$0.01 par value, 5,000,000	\$ 14,728	\$ 16,156
shares authorized, none issued Private placement units of common stock and		
warrants	883,200	883 <b>,</b> 200
Private placement units subscription receivable	(73,500)	(73,500)
Additional paid-in capital	1,288,005	5,741,577
Stock subscription receivable		
Deficit accumulated during development stage	(1,626,872)	(1,626,872)
	\$ 485,561	\$ 4,940,561
	========	========

(1) The number of shares outstanding at September 30, 2001, excludes 420,920 shares of common stock issued after September 30, 2001 through November 21, 2001. Also excluded are: (i) 689,300 shares issuable on exercise of warrants sold in our terminated private placement; (ii) 400,000 shares (including 200,000 warrant shares) issuable on exercise of the option granted to an investor in our terminated private placement to purchase an additional 200,000 units; (iii) 557,801 shares issuable on exercise of warrants granted to certain of our holders of convertible notes in connection with their early conversion of the notes; and (iv) 200,000 shares issuable on exercise of a non-qualified stock option granted to one of our directors. For details about the warrants and investor option, see "Plan of Operation -- Liquidity and Capital Resources," above. For details about the director option, see "Management -- Compensation of Directors and Advisors," below.

#### SELECTED FINANCIAL DATA

The income statement data for the period from July 10, 2000 (inception) through December 31, 2000, and balance sheet data at December 31, 2000, are derived from our financial statements that have been audited by Scillia Dowling & Natarelli LLC, independent auditors, and are qualified by reference to those audited financial statements and related notes to the statements, which are included elsewhere in this prospectus. The income statement data for the nine months ended September 30, 2001, and balance sheet data at September 30, 2001, are derived from unaudited financial statements which are included elsewhere in this prospectus. The unaudited financial statements include all adjustments, consisting of normal recurring accruals, which our management considers necessary for a fair presentation of the information set forth in those statements. Operating results for the nine months ended September 30, 2001, are not necessarily indicative of the results that may be expected for the year ending December 31, 2001. You should read the data set forth below in conjunction with "Plan of Operation," above, and the financial statements and notes included in this prospectus.

	July 10, 2000 (inception) to December 31, 2000	(Unaudited Nine Months E September 30,
Income Statement Data		
Revenue	\$	\$
Net loss	\$ (112,927)	\$ (1,513,9
Net loss per share	\$ (0.01)	\$ (0.
Outstanding Shares-Basic	11,119,203	13,074,4
	December 31, 2000	(Unaudit September 30
Balance Sheet Data		
Total assets	\$ 227,940	\$ 1,170,5
Working capital	\$ 157,378	\$ 378,1
Long-term debt	\$ 284,500	\$ 195,0

Period from

\$ (103,927)

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Stockholders' (deficiency)/equity

485,5

Initial Corporate Organization, Acquisition and Merger

We were incorporated as "DTR-Med Pharma Corp." under Nevada law in January 2001 for the purpose of acquiring all the outstanding stock of our predecessor, Pro-Pharmaceuticals, Inc., which was a Massachusetts corporation engaged in a business we desired to acquire. From our incorporation until just before the acquisition, we were a wholly-owned subsidiary of Developed Technology Resource, Inc., a Minnesota corporation whose common stock is publicly traded on the Over-the-Counter Bulletin Board. In exchange for 1,221,890 shares of our common stock, Developed Technology transferred to us contractual rights that are described below under "Business of Pro-Pharmaceuticals -- Cancer Detection Technology." As part of that process, Developed Technology distributed its holdings of our common stock to its shareholders of record as of May 7, 2001. In anticipation of the acquisition of the Massachusetts company, we changed our name to "Pro-Pharmaceuticals, Inc."

On May 15, 2001, we acquired all of the outstanding common stock of the Massachusetts corporation. We acquired these shares in exchange for 12,354,670 shares of our common stock. As a result, that corporation became our wholly owned subsidiary, and its shareholders through an exchange owned approximately 91% of the outstanding shares of our common stock, with the Developed Technology shareholders owning the remaining 9%. See "Security Ownership of Certain Beneficial Owners and Management" for information about the ownership of our common stock. After the acquisition, we merged with the Massachusetts corporation and are the surviving corporation in the merger. The transaction has been accounted for as a reverse acquisition in which the predecessor corporation purchased our outstanding shares, due to the change in control of the entity. The business combination has been accounted for using purchase accounting, with the assets and liabilities of the acquired company being recorded at fair value.

Concurrent with the acquisition, all of our original officers and directors resigned and were succeeded by the officers and directors of the predecessor Massachusetts corporation, except for Peter Hauser, who has served a director from our incorporation in January 2001. He had also served as Vice President from that time until the acquisition.

As required by the stock exchange agreement that effected the acquisition, we filed a registration statement in June 2001 on Form 10-SB with the Securities and Exchange Commission in order to register our common stock under the Securities Exchange Act of 1934. The registration of our common stock under the Exchange Act became effective on August 13, 2001. Our articles of organization provide that our common stock may not be sold without our approval until the earlier of May 1, 2003 or the 90th day after the date our common stock is registered under the Securities Exchange Act of 1934. Accordingly, our common stock became eligible for transfer, subject to applicable federal and state securities law requirements, as of November 11, 2001. We anticipate that we will retain a market maker to apply for trading of our common stock on the Over-the-Counter Bulletin Board following effectiveness of this registration statement.

We are continuing the business of Pro-Pharmaceuticals (Massachusetts), which has been attempting to develop a technology that will reduce the toxicity and improve the efficacy of current drug therapies, including cancer chemotherapies, by combining the drugs with a number of specific carbohydrate compounds. This is now the principal focus of our business, and is the basis for the business discussion included in this registration statement.

Our address is 189 Wells Avenue, Suite 200, Newton, Massachusetts 02459. Our telephone number is (617) 559-0033, fax number is (617) 928-3450, e-mail address is Plattpharma@aol.com, and our website address is www.pro-pharmaceuticals.com.

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Business of Pro-Pharmaceuticals

Overview

We are an early-stage research and development pharmaceutical company that intends initially to identify, develop and seek regulatory approval of technology that will reduce toxicity and improve the efficacy of currently existing chemotherapy drugs by combining the drugs with a number of specific carbohydrate compounds. Our fundamental objective is to increase the body's tolerance to the drugs by enabling delivery of the drugs while protecting healthy tissue. This would also permit use of larger doses of the drugs, since current dosages are generally limited due to concerns relating to their toxic effects on healthy cells. Our carbohydrate-based drug delivery system may also have applications for drugs now used to treat other diseases and chronic health conditions.

In technical terms, we seek to "reformulate" existing cancer chemotherapy drugs with non-toxic carbohydrate-based compounds that recognize and adhere to specific binding sites on the surface of cancer cells. Reformulation of chemotherapy drugs already approved by the U.S. federal Food and Drug Administration has the following benefits for our business:

- Our carbohydrate-based drug delivery system requires less time for development and FDA approval, and thus reaches the market sooner, because the active chemotherapy drugs are already approved and in widespread use for cancer treatment.
- o We expect fewer risks in drug development because our carbohydrate-based compounds would be combined with drugs already in widespread use. Use of carbohydrate compounds with increased capacity to bind to receptors only on cancer cells and combining the drug with a harmless carbohydrate polymer will reduce the toxic effect on healthy cells and permit better calibration (including possible increase) of dosages to diseased tissue.
- o We foresee a ready demand for chemotherapy that is less toxic and has greater efficacy. We believe the pharmaceutical industry would respond favorably to drug delivery systems to upgrade chemotherapies which patients would tolerate more easily. The industry would likely also be receptive to patent-protected drug delivery systems that "attach" to chemotherapies whose patent protection has expired.
- o We believe that the development of drug delivery systems to upgrade these widely used drugs can be accomplished with much less investment compared to the typical expenditures made by large pharmaceutical companies for a new drug launch.

Cancer and Therapy Issues

Cancer is a disease characterized by uncontrolled growth and spread of abnormal cells. The disease may be caused by patient-specific factors such as genetic predisposition, immune deficiency, hormones, diet and smoking, or external factors such as exposure to a toxic environment. It is the second leading cause of death in the United States, resulting in over 550,000 deaths annually. The National Cancer Advisory Board reports that more than 8 million persons in the U.S. have cancer. Estimates claim that approximately one in three Americans will be diagnosed with the disease their lifetime. About 1.2 million new cases are diagnosed in the U.S. each year. As populations age in the U.S.,

Canada and other industrialized nations, the incidence of the disease is expected to increase. About 6 million persons worldwide die annually from cancer.

The most widely used methods to treat cancer are surgery, radiation and chemotherapy. Cancer patients often receive a combination of these treatments, and about half of all patients receive chemotherapy. Both radiation and chemotherapy have significant limitations that often result in treatment failure. In the case of chemotherapy, these limitations include:

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- Toxicity. Most chemotherapy agents kill cancer cells by disrupting the cell division process. Cells are killed once they begin to undergo division and replication. Although these agents are effective on cancer cells, which generally grow rapidly through cell division, they also kill healthy non-cancerous cells as these cells undergo ordinary division. This is particularly apparent in fast-growing normal cells, such as blood cells forming bone marrow, in the digestive tract, hair follicles, and reproductive cells. As the chemotherapy harms healthy tissue, the effectiveness of the drug is limited because dosage levels and treatment frequency cannot exceed tolerance levels for noncancerous cells. Moreover, the chemotherapy regimen often dramatically diminishes the quality of a patient's life through its physical and emotional side effects.
- Inability to Selectively Target Diseased Cells. The administration of chemotherapy occurs in such a way that the drug reaches both healthy and diseased tissue. Normal cells are generally as receptive as tumors to the toxic effects of chemotherapy. Without the ability to target the drug exclusively to cancerous tissue, chemotherapy dosages must be kept within a range that healthy tissue can tolerate, thus reducing the optimal effectiveness of chemotherapy on diseased tissue.

Our Business Strategy and Initial Objectives

We seek to increase the effectiveness of current cancer treatment and other drugs. The initial objectives of our business strategy are as follows:

- Verify and extend the carbohydrate-based drug enhancement concept encompassing our approach for developing novel cancer chemotherapy products.
- o Expand and enhance clinical applications of at least five widely used chemotherapy drugs (5-Fluorouracil, Adriamycin, Taxol, Cytoxan and Cisplatin) by combining them with our carbohydrate-based drug delivery system.
- Demonstrate the safety and efficacy of such product candidates by means of preclinical evaluation and submitting investigational new drug ("IND") applications to the FDA.
- Accelerate commercialization by identifying products that qualify for fast-track designation by the FDA (further described below). We plan to develop products to be used in treatment of types and stages of cancer for which treatments are now inadequate. The FDA has adopted fast-track and priority procedures for accelerating the approval of oncology agents addressing such needs, potentially reducing the time required to bring new drugs to market. Once approved, we would seek to expand the market potential of our products by seeking approval for

indications in larger cancer patient populations.

- O Leverage our carbohydrate-based drug enhancement technology by applying it to other FDA-approved drugs, including drugs for conditions or ailments other than cancer, that would benefit from reduced toxicity and/or greater efficacy. This strategy would enable us to increase the portfolio of drugs to which our technology may be applied without corresponding development risk and expense of creating new drugs.
- o Apply our drug enhancement system with the aim of extending the patent life of current drugs, or in some cases drugs with expired patents, creating new patent protection. For example, the patent protections of the five cancer drugs with which we propose to work have all expired or long been in the public domain. Non-cancer drugs whose patents have expired, and that we might apply our carbohydrate-based drug enhancement

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technology to include: Prozac (anti-depressant manufactured by Eli Lilly and Company); Prilosec (anti-ulcerative manufactured by AstraZenaca PLC); and Zoloft (anti-depressant manufactured by Pfizer Inc.).

Drug Delivery Technologies

#### General

The ultimate objective of enhanced drug delivery is to control and optimize the localized release of a drug at the target site and rapidly eliminate from the body the portion of the drug that was not delivered to the diseased tissue. Conventional drug delivery systems such as controlled release, sustained release, transdermal systems, and others are based on a physical erosion process for delivering active product into the systemic circulation over time with the objective of improving compliance by patients with a therapy regimen. These systems do not address the biologically important issues such as site targeting, localized release and elimination of undelivered drug from the body. The major factors that impact the achievement of this ultimate goal are:

- o Physical characteristics of a drug. These characteristics affect, among other things, the drug's interactions with the intended pharmacological target sites and undesired areas of toxicity; and
- Biological characteristics of the diseased area. These characteristics impact the ability of a drug to selectively interact with the intended target site to allow the drug to express the desired pharmacological activity.

Both of these factors are important in increasing efficacy and reducing toxicity of cancer drugs. Biotechnology affords a new opportunity in drug delivery techniques by taking advantage of biological mechanisms such as drug-cell recognition and interactions, and particular physical characteristics of cancerous tissue.

Our Focus: Carbohydrate-Based Drug Enhancement Technology

We are attempting to develop a carbohydrate-based drug delivery technology to direct cancer drugs more selectively to tumor tissue so as to reduce the toxic side effects and improve the tumor reduction capacity of chemotherapy

drugs now in use. Carbohydrates are found in the structural elements of cell walls and, among other functions, serve as recognition elements in biomolecules, enabling molecule-cell recognition, and hence, molecular targeting. The dense concentration of chemical functional groups within carbohydrates compared to other chemicals suits them for use in cell recognition applications in biological systems.

Our drug enhancement technology is intended to take advantage of the following biological mechanisms to improve drug delivery:

- o Disease-specific carbohydrate recognition; and
- o Enhanced permeability and retention in tumors.

Our technology does not change the chemistry of the drugs themselves, but rather "attaches" cancer drugs to proprietary carbohydrate compounds, which interact with sugar-specific proteins on the surface of the tumor cell. Because of these cell surface interactions, we believe that these compounds will increase cell permeability, resulting in increased targeted absorption of drugs by cancer cells. These cell surface interactions may also reduce the cells' ability to adhere to each

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other as well as to normal tissue, resulting in diminished ability of cancer cells to metastasize, or spread to other tissue systems.

Our preliminary studies have led to the identification of certain mannans, a group of polysaccharides, as a potential drug delivery system. Polysaccharides are molecules consisting of one or more types of sugars. In the case of mannans, the principal component is the sugar mannose, which is similar in many respects to glucose. While mannans can be isolated from plant or microbial sources, we use mannans isolated from plants. We believe that a mannan with suitable chemical structure and composition, when attached to or combined with the active agent of a chemotherapy drug, increases cellular membrane fluidity and permeability, thereby assisting delivery of the drug. Also, our studies have shown that mannans of a certain structure may be able to protect healthy tissue from the toxic effects of chemotherapy drugs, and also may be able to increase therapeutic efficacy of such drugs.

### Initial Chemotherapy Applications

We believe that our carbohydrate-based drug enhancement technology applies to essentially any oncology drug whose delivery to the target can be improved by utilizing sugar-specific recognition at the cancer cell surface. Initially, we are studying the effect of our carbohydrate-based system on the toxicity and efficacy of selected cancer drugs. We have conducted preliminary studies that indicate that certain of our mannans, when combined with some of these drugs, may significantly reduce the toxic effects of the drugs and may also increase therapeutic efficacy of such drugs.

Our initial program is designed to be "risk-contained" in that it will focus on proven drugs for which there are already a great deal of data on their therapeutic efficacy and toxicity, along with an accumulated knowledge of their limitations. We intend to apply our drug delivery technology initially to five widely used chemotherapy agents: 5-Fluorouracil, Adriamycin, Taxol, Cytoxan and Cisplatin. Each of these drugs is among the most popular drugs used in cancer chemotherapy treatment in the United States, and for each of these drugs there is a strong need for improving their therapeutic efficacy and decreasing their toxicity.

- 5-Fluorouracil (5-FU) is a fluorinated pyrimidine (a nucleic acid component). It interferes with the synthesis of DNA and inhibits the formation of RNA. Since DNA and RNA are essential for cell division and growth, the effect of 5-FU provokes unbalanced growth and death of the cell. The effect of DNA and RNA deprivation is most marked on those cells which grow more rapidly and which take up the 5-FU at a more rapid rate, such as cancer cells. 5-FU is effective against cancers of the colon, rectum, breast, stomach and pancreas. This drug is also toxic, resulting in side effects such as nausea, vomiting, mouth sores, gastrointestinal ulceration and bleeding, loss of hair, skin darkening and fatigue. 5-FU is manufactured by Roche Laboratories for intravenous administration. Originally patented in the late 1950s, its patent protection has expired.
- o Adriamycin (generic name -- doxorubicin hydrochloride) is a cytotoxic agent that selectively kills malignant cells and causes tumor regression. It binds to the DNA, and presumably inhibits nucleic acid synthesis. It is used to treat, among others, leukemia, cancers of the breast, ovaries, bladder, stomach and thyroid, as well as Hodgkin's and non-Hodgkin's lymphoma. Adriamycin is toxic, resulting in side effects such as nausea, vomiting, loss of hair, mouth sores, colon ulceration and heart damage. It is manufactured by Pharmacia Upjohn for intravenous administration. Originally patented in 1971, its patent protection has expired.

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- Taxol (generic name -- paclitaxel) is a relatively new anti-leukemic and anti-tumor agent, possessing a cytotoxic activity. It suppresses cell division by binding to so-called microtubules that form in a cell's nucleus to help move the chromosomes around during the division process. Taxol is most effective against ovarian and advanced breast cancers, particularly after failure of standard chemotherapy. Studies indicate that it might be effective against leukemia, lung carcinoma, colon carcinoma, renal carcinoma, melanoma, and CNS carcinoma. Taxol is toxic, and patients receiving it often develop problems ranging from rashes, drop in blood pressure and anemia to major breathing problems, hives and/or fluid buildup around the heart and bone marrow suppression. Almost all patients experience hair loss from Taxol, and some patients experience severe hypersensitivity reactions to Taxol. It is manufactured by Bristol-Myers-Squibb Company for intravenous administration. We believe that there are no patents covering the composition of Taxol (paclitaxel).
- O Cytoxan (generic name -- cyclophosphamide) has action leading to cross-linking of RNA of tumor cells, and thereby interferes with the growth of susceptible rapidly proliferating malignant cells. It is effective against a range of cancers, such as malignant lymphomas, Hodgkin's disease, various leukemias, and cancer of the breast and ovaries. This drug is toxic, with side effects including nausea, vomiting, anorexia, diarrhea, skin rash and darkening and, in extreme cases, heart damage or failure, and secondary malignancies. It is manufactured by Bristol-Myers-Squibb Company for intravenous and oral administration. We believe that there are no patents covering the composition of Cytoxan (cyclophosphamide).
- o Cisplatin appears to act by inhibiting DNA synthesis. It is effective against metastatic testicular and ovarian tumors (typically in combination with other chemotherapeutic agents, such as Cytoxan,

above), and advanced bladder cancer. This drug is toxic, with side effects including renal toxicity, nausea, vomiting, anorexia, diarrhea and anemia. It is manufactured as PLATINOL(R) by Bristol-Myers-Squibb Company for intravenous injection. We believe that there are no patents covering the composition of Cisplatin.

#### Preclinical Animal Studies

As discussed below, using independent laboratories we have conducted preclinical animal experiments to study the toxicity and efficacy of 5-Fluorouracil (5-FU) and Adriamycin in combination with our mannan compounds.

### Toxicity Studies

Results of one toxicity study conducted in early 2001 indicate that one of our mannan compounds may significantly decrease the toxicity of 5-FU. Ten groups of five animals each were used. In five groups, treated respectively with a placebo and one of four different mannans provided by us, the animals showed no signs of toxicity. That was expected because the animals were not receiving the toxic drug, and the mannans were not expected to be toxic at all. In four groups, treated respectively with 5-FU alone and 5-FU in combination with either of three of the mannans, the animals showed signs of severe toxicity. In one group, treated with 5-FU in combination with the fourth mannan, no clinical signs of toxicity were observed. This provides a preliminary indication of potential reduction in cancer drug toxicity by a carbohydrate-based addition to the cancer drug.

A second, similar study, also conducted in early 2001, was performed to test a potential reduction of toxicity of another anticancer drug, Adriamycin, in combination with each of two mannan compounds selected for the study. Results indicate that one of the mannan compounds

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may decrease the toxicity of Adriamycin. In two groups, treated with Adriamycin alone and Adriamycin in combination with one mannan, the animals showed signs of severe toxicity. In one group, treated with the same amount of Adriamycin in combination with the second mannan, four out of the five animals in the group did not show any clinical signs of toxicity. Again, this provides a preliminary indication of potential reduction in cancer drug toxicity by a carbohydrate-based addition to the cancer drug. The fact that two different cancer drugs with chemically unrelated structures showed a marked reduction of their toxicity in combination with particular mannans indicates that there might be some fundamental underlying biological reasons, related to the mannans rather than to the drugs, for the reduction in toxicity.

The above toxicity studies were conducted by Toxikon Corporation, a comprehensive compliance FDA-registered service testing laboratory in Bedford, Massachusetts, that is not affiliated with Pro-Pharmaceuticals. Please see " -- Research" below, for further information about Toxikon Corporation.

In four subsequent preclinical experiments conducted in June and September 2001, we studied on larger animals the toxicity reduction of 5-FU in combination with the same mannan that demonstrated toxicity reduction in the prior 5-FU study. These experiments were performed in accordance with FDA guidelines and recommendations on rats (acute and long-term toxicity study) and dogs (acute and long-term toxicity study) measuring the effect of the 5-FU/mannan combination on blood structure and survival of these animals. Preliminary results indicate that the 5-FU/mannan combination decreased toxicity using this measure because it resulted in lower animal mortality and decreased loss of blood structure

components in comparison to the results of tests which administered 5-FU alone.

These four experiments were conducted by Redfield Laboratories, Inc., based on Redfield, Arkansas and licensed by the U.S. Department of Agriculture to conduct research in laboratory animals. Testing conditions at Redfield Laboratories are in compliance with the federal Animal Welfare Act. Redfield Laboratories is not affiliated with Pro-Pharmaceuticals.

Efficacy Study

A preliminary study was performed to test a potential change in therapeutic efficacy of 5-FU in a combination with that same mannan that decreased toxicity of the drug in healthy animals (see the first study described in " -- Toxicity Studies," above). The study was motivated by the desire to test the possibility that the mannan might diminish both toxicity and efficacy in parallel, if the mannan were merely competing with 5-FU for binding with cells, healthy or cancerous. Results of the study demonstrated, however, that the same mannan that may decrease toxicity of 5-FU may also increase efficacy of the drug when the drug combined with mannan is administered into cancer-carrying animals. In this study, we ascertained a decrease in tumor size following administration of 5-FU alone as well as administration of the 5-FU/mannan combination. When the 5-FU/mannan combination was administered, the time for the tumor to quadruple in size in the animals increased from 24 days (5-FU alone administered) to 56 days (5-FU/mannan combination administered) relative to 12 days for control animals (no drug administered).

The above efficacy study was conducted by Southern Research Institute in Birmingham, Alabama. Southern Research Institute is an independent, not-for-profit contract research organization that is not affiliated with our company. Please see " -- Research" below, for further information about Southern Research Institute.

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#### Carbohydrate-Cancer Drug Formulations

We are currently developing formulations of carbohydrates linked to anti-cancer drugs. We have chemically synthesized two novel products that are carbohydrate derivatives of Adriamycin, and have conducted preclinical animal experiments, studying both toxicity (on healthy animals) and efficacy (on cancer-carrying animals). Preliminary results of these experiments indicate that both of the synthesized carbohydrate-Adriamycin compounds are significantly less toxic compared with the original Adriamycin, and demonstrate therapeutic efficacy as well. These studies were conducted at the Academy of Medical Sciences, Moscow, Russia.

Although the foregoing studies are encouraging, the results achieved in preclinical studies with animals are often not duplicated in human patients. Please see "Risk Factors -- Our product candidates will be based on novel technologies" above.

Cancer Detection Technology

We have an indirect royalty interest in a cancer detection technology that may be applied to the detection of soft tissue nodules in human organs, and may thus assist in the detection of cancerous tissue. A diagnostic system has been developed which is based on this detection technology. This system uses pressure to measure the elasticity or hardness of soft tissue, and, through digitization, provides a clinician with an image of the size and location of nodules in the

tissue. While the detection technology is currently being focused on the development of a prostate imaging system, the technology is also believed to be applicable to the detection of nodules or hardness in the breast.

The detection technology is substantially covered by three United States patents: Patent No. 5,265,612 entitled "Intercavity Ultrasonic Device for Elasticity Imaging"; Patent No. 5,524,636, dated June 11, 1996 entitled "Method and Apparatus for Elasticity Imaging"; and Patent No. 5,785,663 dated July 28, 1998, entitled "Method and Device for Mechanical Imaging of Prostate."

The detection technology is owned, and primary development efforts are being conducted, by ArMed, Inc., a Delaware corporation (formerly ArMed LLC, a Delaware limited liability company). Artann Corporation, a New Jersey corporation, and an earlier owner and developer of the detection technology, transferred the detection technology to ArMed, Inc. in 1996, and in return received a license to use, develop, manufacture and market a home use breast cancer system utilizing the detection technology.

Artann Corporation entered into an "Agreement for Transfer of Patent and Proprietary Rights" dated September 5, 1995, as amended on August 29, 1996, with our former parent company, Developed Technology. We refer to that agreement as the "royalty agreement" in this section. We received our rights under the royalty agreement by assignment from Developed Technology on April 23, 2001. Armen P. Sarvazyan is the original inventor of the detection technology, is the principal shareholder of Artann Corporation, and is also a party to the royalty agreement. Sarvazyan and Artann Corporation, combined, have approximately a 9.5% equity and voting interest in ArMed, Inc., on a fully diluted basis.

The royalties which we have a right to receive under the royalty agreement are based on the gross revenues of Artann Corporation and Sarvazyan. Those gross revenues, if generated, will be obtained by Artann Corporation from (i) the sale of home use breast cancer detection systems, utilizing the detection technology, (ii) the licensing or assignment to third parties of the rights to manufacture and sell breast cancer detection systems utilizing the detection technology, and (iii) distributions made by ArMed, Inc. to Artann Corporation. The royalty computation is complex and not readily subject to description, and varies significantly depending upon the specific application of the detection technology.

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We do not anticipate receiving any revenue under the royalty agreement for at least two years, and we do not expect any revenue we do receive to be substantial. An independent appraisal of our royalty interest under the royalty agreement was obtained in March 2001. That appraisal established a fair market value of our royalty interest at \$107,000.

We may exchange our royalty interest for a direct equity interest in ArMed, Inc. We cannot predict whether our royalty interest will ever result in any revenues to us.

Patents and Proprietary Rights

We have two pending utility patent applications and one provisional patent application in the United States. The patent applications cover methods and compositions for reducing side effects in chemotherapeutic formulations, and improving efficacy and reducing toxicity of chemotherapeutic agents. One of our utility patents is filed worldwide under the Patent Cooperation Treaty.

A provisional patent application is not actually reviewed by the U.S.

Patent and Trademark Office. Rather, it is used to establish a filing, or priority, date for either a U.S. utility patent application, which is subject to review, or a Patent Cooperation Treaty application, which is subject to an initial search and a further review upon request. In order to retain the benefits of the initial filing or priority date, the inventor must file a utility application with the U.S. Patent and Trademark Office, or an application under the Patent Cooperation Treaty, within one year of the original filing date of the provisional application. Otherwise, the filing, or priority, date will be lost.

We intend to file additional patent applications when appropriate, with respect to improvements in our core technology and to specific products and processes that we develop. There can be no assurance that any patents will issue from any present or future applications or, if patents do issue, that such patents will be issued on a timely basis or that claims allowed on issued patents will be sufficient to protect our technology. Our intellectual property is subject to other risks, including potential patent challenges and possible lack of protection. Please see "Risk Factors -- Our competitive position depends on protection of our intellectual property" above, for additional discussion of risks related to intellectual property.

We filed with the U.S. Patent and Trademark Office (PTO) applications to register the following trademarks/service marks: ADVANCING DRUGS THROUGH GLYCOSCIENCE; GLYCO-UPGRADE; and PRO-PHARMACEUTICALS, INC. The PTO generally issues an office action several months after an application is filed which reports on its initial determination of whether a mark is registrable under the federal trademark statute. In November 2001, the PTO informed us that two of these marks, ADVANCING DRUGS THROUGH GLYCOSCIENCE, and GLYCO-UPGRADE, have been approved for publication. Unless an opposition to registration is timely filed, the PTO will register these marks for our use.

#### Research

We anticipate that our focus will be on design and analysis of carbohydrate-based drug enhancement systems. We do not anticipate building in-house research or development facilities, or hiring staff to conduct those activities. As we have done to date, we will have our pre-clinical testing conducted by outside laboratories.

Our early stage research was conducted by Toxikon Corporation, a comprehensive compliance FDA-registered service testing laboratory in Bedford, Massachusetts, that is not affiliated with Pro-Pharmaceuticals. Toxikon's laboratory is ISO-9001 certified and EN-45001 approved, meaning that it complies with quality management standards as established by the International Organization for Standardization and other international organizations.

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Our current research on toxicity and efficacy of several chemotherapy drugs both alone and in combinations with our mannans on cancer-carrying animals is being conducted by Southern Research Institute in Birmingham, Alabama. Southern Research Institute is an independent, not-for-profit contract research organization that is not affiliated with our company.

If we develop products eligible for clinical trials, we will contract with an independent clinical research organization to design the trial protocols and arrange for and monitor the clinical trials. We also intend to rely on academic institutions or clinical research organizations to conduct, supervise or monitor some or all aspects of clinical trials involving our products. In addition, certain clinical trials for our products may be conducted by

government-sponsored agencies and consequently will be dependent on governmental participation and funding. Our dependence on third-party researchers will involve risks including lessened control over the timing and other aspects of any clinical trials, since we will not be conducting them on our own. Please see "Risk Factors -- We have no experience in clinical trials," above, for additional discussion of risks related to our research.

We do not intend to manufacture our products. We anticipate that any products we develop will be manufactured by subcontractors. Please see "Risk Factors -- We will depend on third parties to manufacture and market our products," above, for additional discussion of risks related to contract manufacturing.

#### Manufacturing and Marketing

We are a development company and do not have, or intend to obtain, internal facilities for the manufacture of any of our products for clinical or commercial production. In order to have our products manufactured, we will initially need to develop relationships with third-party manufacturing resources, enter into collaborative arrangements with other parties that have established manufacturing capabilities or elect to have other third parties manufacture our products on a contract basis. Later we would propose to have our products manufactured and marketed pursuant to licensing agreements as discussed below.

We also have no marketing infrastructure, and we do not intend to develop a sales and marketing staff to commercialize pharmaceutical products. If we develop products eligible for commercial sale, we will need to rely on third parties such as licensees, collaborators, joint venture partners or independent distributors to market and sell those products. Our dependence on third-party manufacturers and marketers will involve risks relating to our lessened control, and other risks including those discussed in "Risk Factors -- We will depend on third parties to manufacture and market our products," above.

We currently envision having our manufacturing and marketing operations conducted pursuant to license agreements that we would negotiate with pharmaceutical companies with respect to manufacturing and marketing of their "upgraded" drugs. While we presently contemplate offering the rights to manufacture and market an "upgraded" drug to the original pharmaceutical company that developed the drug, we will evaluate other manufacturing and marketing arrangements as well.

### Competition

We expect to encounter significant competition for the principal drug delivery systems we plan to develop. Companies that complete clinical trials, obtain required regulatory approvals and commence commercial sales of their products before their competitors may achieve a significant competitive advantage. Accordingly, the relative speed with which we and any future collaborators

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can develop products, complete preclinical testing and clinical trials and approval processes, and supply commercial quantities of the products to the market are expected to be important competitive factors. A number of biotechnology and pharmaceutical companies are developing new drug delivery systems for the treatment of the same diseases being targeted by us. In some instances, such products have already entered late-stage clinical trials or received FDA approval. Significant levels of research in biotechnology, medicinal chemistry and pharmacology occur in academic institutions,

governmental agencies and other public and private research institutions. These entities have become increasingly active in seeking patent protection and licensing revenues for their research results. They also compete with us in recruiting and retaining skilled scientific talent. Please see "Risk Factors -- We face intense competition in the biotechnology and pharmaceutical industries," above, for additional discussion related to our current and potential competition.

Our potential competition includes other companies developing drug delivery systems based on carbohydrates, as well as companies developing drug delivery systems based on other polymers. The principal competitors in the polymer area are Cell Therapeutics, Access Pharmaceuticals, Daiichi, Enzon and Pharmacia which are developing alternate drugs in combination with polymers. We believe we are the only company conducting research on mannan-based drug delivery systems.

In addition, we face competition with technologies other than polymer-based delivery technologies. We believe that the principal current competitors to polymer-based targeting technology fall into two categories: monoclonal antibodies and liposomes. A number of companies are developing or may in the future engage in the development of products competitive with our drug delivery system. Several companies are working on targeted monoclonal antibody therapy including Bristol-Myers Squibb, Centocor, GlaxoSmithKline, Imclone and Xoma. Currently, liposomal formulations being developed by Nexstar (acquired by Gilead Sciences), The Liposome Company (acquired by Elan Corporation) and Sequus Pharmaceuticals (acquired by Alza Corporation), are the major competing intravenous drug delivery formulations which deliver similar drug substances. A number of companies are developing or evaluating enhanced drug delivery systems. We expect that technological developments will occur at a rapid rate and that competition is likely to intensify as various alternative delivery system technologies achieve similar if not identical advantages.

We believe that our ability to compete successfully will be based on our ability to create and maintain scientifically advanced technology, develop proprietary products, attract and retain scientific personnel, obtain patent or other protection for our products, obtain required regulatory approvals and manufacture and successfully market our products either alone or through outside parties.

### Government Regulation

The research, development, testing, manufacture, labeling, promotion, advertising, distribution, and marketing, among other things, of our products are extensively regulated by governmental authorities in the United States and other countries. In the United States, the Food and Drug Administration (FDA) regulates drugs under the Federal Food, Drug, and Cosmetic Act and its implementing regulations. Failure to comply with the applicable U.S. requirements may subject us to administrative or judicial sanctions, such as FDA refusal to approve pending new drug applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, and/or criminal prosecution. Please see "Risk Factors — We will need regulatory approvals to commercialize our products," above, for additional discussion of risks related to regulatory compliance.

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#### Drug Approval Process

No drug may be marketed in the U.S. until the drug has received FDA approval. We have not yet submitted an application for approval for any of our product candidates. The steps required before a drug may be marketed in the U.S.

#### include:

- o preclinical laboratory tests, animal studies, and formulation studies
- o submission to the FDA of an investigational new drug application, or IND, for human clinical testing, which must become effective before human clinical trials may begin
- o adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for each indication
- o submission to the FDA of a New Drug Application, or NDA
- o satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Procedures established by the FDA ("cGMP") and
- o FDA review and approval of the NDA.

Preclinical tests include laboratory evaluation of product chemistry, toxicity, and formulation, as well as animal studies. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND, which must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about issues such as the conduct of the trials as outlined in the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. We cannot be sure that submission of an IND will result in FDA allowing clinical trials to begin.

Clinical trials involve the administration of