1 As filed with the Securities and Exchange Commission on December 20, 1996 Registration No. 33-91228 \_\_\_\_\_ SECURITIES AND EXCHANGE COMMISSION WASHINGTON, D.C. 20549 -----AMENDMENT NO. 1 т0 POST-EFFECTIVE AMENDMENT NO. 1 TO FORM S-1 ON FORM S-3 REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933 CYTOTHERAPEUTICS, INC. (Exact name of registrant as specified in its charter) DELAWARE 2836 94-3078125 (State or other jurisdiction (Primary Standard of incorporation or Industrial Classification (I.R.S. Employer Identification No.) Code Number) organization) TWO RICHMOND SQUARE, PROVIDENCE, RHODE ISLAND 02906, (401) 272-3310 (Address, including zip code, and telephone number, including area code, of registrant's principal executive offices) FREDERIC A. EUSTIS, III, ESQ. Secretary CYTOTHERAPEUTICS, INC. Two Richmond Square Providence, Rhode Island 02906 (401) 272-3310 (Name, address, including zip code, and telephone number, including area code, of agent for service) -----Copy to: GEOFFREY B. DAVIS, ESQ. ROPES & GRAY 30 Kennedy Plaza Providence, Rhode Island 02903 (401) 455-4400 Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this Registration Statement. \_\_\_\_\_ SUBJECT TO COMPLETION DATED DECEMBER 20, 1996

CYTOTHERAPEUTICS, INC.

2,434,500 SHARES OF COMMON STOCK

This Prospectus relates to the issuance by CytoTherapeutics, Inc. (the "Company") of shares of its Common Stock, \$.01 par value ("Common Stock") from time to time upon the exercise of a Common Stock Purchase Warrant (the "Warrant") issued by the Company. The Warrant entitles the holder, subject to adjustment as set forth in the Warrant, to purchase up to 434,500 shares of Common Stock at a price of \$8.00 per share, at any time through April 30, 2000, when the Warrant expires. The Warrant is nontransferable and, subject to certain exceptions, may be redeemed by the Company upon 30 days written notice at a price of \$.05 per warrant share, if the average last sale prices of the Common Stock (as reported by the Nasdaq National Market) exceeds \$12.00 per share for any period of thirty (30) consecutive trading days ending within thirty (30) days of the notice of redemption. This Prospectus also relates to the issuance by the Company of additional shares of its Common Stock pursuant to the exercise by the holder of the Warrant of certain Additional Antidilution Rights granted pursuant to the Warrant. See "Description of Warrants."

The exercise price of the Common Stock underlying the Warrant and the terms of the Warrant were determined by negotiations between the Company and purchaser of the Warrant. The Common Stock of the Company is listed on the Nasdaq National Market under the symbol "CTII." On December 13, 1996, the last reported sale price for the Common Stock as reported by the Nasdaq National Market was \$8.875.

The shares of Common Stock offered hereby are offered directly by the Company. All expenses of the Offering will be paid by the Company.

THE SECURITIES OFFERED HEREBY INVOLVE A HIGH DEGREE OF RISK. SEE "RISK FACTORS" BEGINNING ON PAGE 4.

THESE SECURITIES HAVE NOT BEEN APPROVED OR DISAPPROVED BY THE SECURITIES AND EXCHANGE COMMISSION OR ANY OTHER STATE SECURITIES COMMISSION, NOR HAS THE SECURITIES AND EXCHANGE COMMISSION OR ANY STATE SECURITIES COMMISSION PASSED UPON THE ACCURACY OR ADEQUACY OF THIS PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this Prospectus is December \_\_\_, 1996

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### AVAILABLE INFORMATION

CytoTherapeutics, Inc. ("CytoTherapeutics" or the "Company"), is subject to the information requirements of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and, in accordance therewith, is required to file periodic reports, proxy materials and other information with the Securities and Exchange Commission (the "Commission"). Reports, proxy statements and other information can be inspected and copied at the public reference facilities maintained by the Commission at Room 1024, Judiciary Plaza, 450 Fifth Street, N.W., Washington, D.C. 20549, or at its regional offices located at Suite 1400, Northwest Atrium Center, 500 West Madison Street, Chicago, Illinois 60661, and at 7 World Trade Center, New York, New York 10048, and copies of such material can be obtained from the Public References Section of the Commission, 450 Fifth Street, N.W., Washington, D.C. 20549, at prescribed rates. In addition, material that the Company files electronically with the Commission is available at the Commission's Web Site, http://www.sec.gov, which contains reports, proxy and information statements, and other information regarding issuers that file electronically with the Commission.

### INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The following documents filed by the Company with the Commission are incorporated by reference into this Prospectus and made a part hereof:

- (i) Annual Report on Form 10-K for the fiscal year ended December 31, 1995, including portions of the Company's definitive Proxy Statement filed in connection with the Company's 1996 Annual Meeting of Stockholders.
- (ii) Quarterly Reports on Form 10-Q for the quarters ended March 31, 1996, June 30, 1996 and September 30, 1996.
- (iii) Current Report on Form 8-K filed with the Commission on July 16, 1996.
- (iv) Current Report on Form 8-K filed with the Commission on December 20, 1996.
- (v) The description of the Company's Common Stock contained in its registration statement on Form 8-A, File No. 1-19871.

All documents filed by the Company pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this Prospectus and prior to the termination of the Offering shall be incorporated by reference into this Prospectus and shall be deemed to be a part of this Prospectus from the date of filing of such documents. Any statement contained in a document incorporated by reference shall be deemed to be modified or superseded for all purposes to the extent that a statement contained in this Prospectus or in any other subsequently filed document which also is or is deemed to be incorporated by reference modifies or supersedes such statement.

The Company will provide, upon request, without charge to each person to whom a copy of this Prospectus has been delivered, a copy of any or all of the documents which have been or may be incorporated in this Prospectus by reference, other than certain exhibits to such documents. Requests for such copies should be directed to: Investor Relations, CytoTherapeutics, Inc., Two Richmond Square, Providence, Rhode Island 02906 (401) 272-3310.

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## THE COMPANY

CytoTherapeutics is a leader in the development of proprietary products and technology designed to deliver therapeutic substances to the central nervous system ("CNS"). The Company's CNS-focused technology is designed to provide controlled, site-specific and safe delivery of a variety of novel therapeutic substances across the blood-brain barrier, potentially overcoming a fundamental obstacle to effective treatment of CNS disease. The Company is currently developing products for the treatment of chronic pain, Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis , with additional research efforts directed to several other CNS disorders. Through its 50% owned Swiss subsidiary, Modex Therapeutiques SA, the Company is also developing applications of its technology to treat diabetes, blood disorders and obesity.

CytoTherapeutics was incorporated under Delaware law in August 1988. The Company's executive offices are located at Two Richmond Square, Providence, Rhode Island 02906, and its telephone number is (401) 272-3310.

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#### RISK FACTORS

Prospective investors in the securities offered hereby should carefully consider the following risk factors, in addition to the other information appearing in this Prospectus. This Prospectus and the documents incorporated by reference into this Prospectus contain forward-looking statements relating to the Company's product development programs, need for and timing of, additional capital, capital expenditures, intellectual property rights, the need for additional facilities and regulatory approvals that involve risks and uncertainties. The Company's actual results may differ materially from the results discussed in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in the following "Risk Factors."

## EARLY STAGE OF DEVELOPMENT; HISTORY OF OPERATING LOSSES

The Company has developed no products, has derived no revenues from the sale of any products and does not expect to generate any such revenues in the near future. Substantially all of the Company's revenues to date have been derived from collaborative agreements, research grants and income earned on invested funds. To achieve profitable operations, the Company, alone or with others, must successfully develop, obtain regulatory approval for, manufacture, market and sell products. There can be no assurance that any of the Company's product development efforts will be successful or, if successful, that required regulatory approvals will be obtained.

The Company had losses from operations of approximately \$15.0 million, \$17.0 million and \$7.6 million for the years ended December 31, 1993, 1994 and 1995, respectively, and had an accumulated deficit of approximately \$68.5 million at September 30, 1996. The Company will continue to incur substantial operating losses in the future as the Company conducts its research, development, clinical trial and manufacturing activities. Such losses may fluctuate significantly from quarter to quarter. There can be no assurance that the Company will achieve revenues from product sales or become profitable. Furthermore, based on changes in the Company's ownership, utilization of net operating loss carryforwards and research and development credits for Federal income tax purposes may be subject to annual limitations.

## FUTURE CAPITAL NEEDS; UNCERTAINTY OF ADDITIONAL FUNDING

The development of the Company's products will require the commitment of substantial resources to conduct the time-consuming research, preclinical development and clinical trials that are necessary for regulatory approvals and to establish production and marketing capabilities if such approvals are obtained. In addition, with respect to certain of the Company's proposed products, the Company believes it may be necessary to access third party technologies which may require substantial funds. The Company will need to raise substantial additional funds to continue its product development efforts and intends to seek such additional funds through partnership, collaborative or other arrangements with corporate sponsors, public or private equity or debt financings, or from other sources. Any equity financing could result in dilution to the Company's then existing shareholders. A large number of biotechnology companies are competing with the Company for access to limited capital. Lack of necessary funds may require the Company to delay, reduce or eliminate some or all of its research and product development programs or to license its potential products or technologies to third parties. No assurance can be given that funding will be available when needed, if at all, or on terms acceptable to the Company.

The Company may also need additional funding earlier than anticipated, and its cash requirements, in general, may vary materially from those now contemplated. Future cash requirements may vary based on changes in the Company's research and development programs, progress in preclinical and clinical testing, the Company's ability to enter into, and perform successfully under, collaborative agreements, competitive and technological advances, the need to contest or obtain proprietary rights owned by third parties, facilities requirements, regulatory approvals and other factors.

## UNCERTAINTIES OF NEW MODE OF THERAPY

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The development of new pharmaceutical products is generally subject to a number of significant risks. Potential products that appear to be promising at an early stage of research or development may not reach the market for a number of reasons. Potential products may prove to be ineffective, have adverse side effects, fail to receive necessary regulatory approvals, fail to gain market acceptance, be difficult or uneconomical to manufacture or market on a commercial scale, be adversely affected by government regulations, government price controls or limitations on reimbursement, be precluded from commercialization by proprietary rights of third parties or be subject to significant competition from other products.

In addition, the Company's proposed products represent a novel therapeutic approach. All of the Company's research and product development efforts are in an early stage and, to succeed, the Company must make significant advances in a number of areas. To the Company's knowledge, no product similar to the Company's proposed products has ever been approved by regulatory agencies or been successfully commercialized. The success of the Company's products will depend upon the Company's ability to demonstrate the commercial validity of encapsulated cell therapy. To do so, the Company must show that its implants, among other things: (i) successfully isolate transplanted cells from the recipient's immune system; (ii) remain biocompatible with the tissue into which they are implanted; (iii) maintain the viability of cells contained within the membrane; (iv) safely permit the therapeutic substances produced by the cells within the membrane to pass through the membrane into the patient; and (v) are sufficiently durable for the intended indication and to allow the implants to be retrieved intact. While the Company believes it has developed implants which demonstrate each of these qualities in animal models and early human testing, a number of its implants have not been successful. The reasons for failure of these implants have not always been definitively identified.

It is expected that the Company's implants may differ substantially from application to application, depending on, among other things, the targeted disease or condition, the site of implantation and the type of encapsulated cell. Even if regulatory approvals can be obtained for one type of implant, there can be no assurance that other implants can be successfully developed and approved.

The Company's proposed products are expected to have high unit costs, and implantation of these products may require costly surgical procedures. The Company's potential products are expected to consist, in part, of living cells, which the Company and medical personnel using the product must keep viable from the time the cells are encapsulated through their distribution and implantation in the patient. There can be no assurance that the medical community or patients will accept the Company's products, even if the Company's products are successfully developed, are shown to be safe and effective in clinical trials and are approved for marketing by the FDA and other regulatory authorities in the United States and abroad.

## UNCERTAINTIES OF CLINICAL DEVELOPMENT

Before obtaining required regulatory approvals for the commercial sale of products, the Company must demonstrate through clinical trials that such products are safe and efficacious for use in each target indication. The Company has limited experience in conducting clinical trials and expects to enter into arrangements with third parties or collaborators for assistance in the conduct of clinical trials. There can be no assurance that the Company will be able to negotiate such arrangements on acceptable terms, if at all, or that such arrangements will be successfully completed. None of the products under development by the Company has received regulatory approval. There can be no assurance that such regulatory approval will be received on a timely basis, if at all, or that necessary clinical trials will commence in the time frames anticipated by the Company, if at all.

The results of preclinical tests, including animal model studies, are not necessarily predictive of the safety or efficacy of a therapeutic candidate in humans, and the results of initial clinical trials will not necessarily predict results that may be obtained from larger-scale, later-stage clinical trials. Further, there can be no assurance that any products developed by the Company will be safe and efficacious in humans, or that the administration to humans of any product under development by the Company will not produce undesirable side effects. The effects of transplanting unencapsulated cells or organs, including their potential to cause tumors, disease, such as bovine spongiform encephalopathy or BSE, or other adverse side effects, are not well understood. As a result, in order to achieve regulatory approval for clinical trials and commercialization of its proposed products, it may be necessary for the Company to demonstrate to a high degree of certainty that its implants will not release the cells they contain and there



can be no assurance that the Company will be able to achieve the necessary level of certainty. Failure to obtain such certainty or the occurrence of such side effects or lack of safety and efficacy could interrupt or delay clinical testing of such products and could ultimately prevent their approval by the FDA or foreign regulatory authorities. Many biotechnology products have failed to demonstrate safety and efficacy in later-stage clinical trials. The Company, its principal investigators, its corporate collaborators or the FDA may suspend clinical trials at any time if it is believed that the patients participating in such trials are being exposed to unacceptable health risks. Even after approval by the FDA and foreign regulatory authorities, products may exhibit adverse side effects that prevent their widespread use, necessitate their withdrawal from the market and subject the Company to liability.

## DEPENDENCE ON OUTSIDE PARTIES

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The Company is dependent on a number of important arrangements with outside parties. The Company's strategy for the research, development, commercialization and marketing of its products contemplates that the Company will enter into various arrangements with corporate sponsors, pharmaceutical companies, universities, research groups and others. The Company, in particular, has licensed technology from Brown University and certain researchers associated with Brown University. Dr. Patrick Aebischer, at the Centre Hospitalier Universitaire Vaudois in Switzerland, has conducted, and is currently conducting clinical trials of the Company's implants, and is also conducting further research sponsored by the Company. There can be no assurance that the Company will be able to continue any arrangements such as its agreements with Brown University, the Centre Hospitalier Universitaire Vaudois, Dr. Aebischer or other institutions or researchers on terms acceptable to the Company, if at all. None of the Company's founding scientists or Scientific Advisory Board members is employed by the Company, and all may have commitments to or consulting contracts with others.

The Company is seeking and expects to seek third party funding through corporate partnerships or similar arrangements for some or all of the research, development, clinical trial and commercialization expenses associated with its products. The Company has established collaborations with Astra AB, Genentech, Inc., and Akzo Nobel Fraser AG, and intends to enter into additional collaborations relating to the research, development and commercialization of its potential products. There can be no assurance that the Company can enter into such additional arrangements on terms acceptable to the Company, or that the Company will successfully fulfill its obligations under any such arrangements. The Company's failure to enter into such arrangements and to continue them on terms acceptable to the Company, or successfully to perform its obligations under such arrangements, could have a material adverse effect on the Company. In addition, there can be no assurance that any funds received under the Company's collaborative arrangements will be sufficient, individually or in the aggregate, to cover the costs incurred by the Company in support of the related collaborative programs. Although the Company believes its collaborative partners would have an economic incentive to succeed in performing their contractual responsibilities, the amount and timing of resources to be devoted to these activities by such partners is not within the control of the Company. There can be no assurance that the interests of the Company will coincide with those of its collaborators or that disagreements over rights to technology or other proprietary information will not occur. If any of the Company's collaborators breaches or terminates its agreement with the Company, or otherwise fails to conduct its collaborative activities in a timely and effective manner, the development or commercialization of the product candidate or research program under such collaborative agreement may be delayed, the Company may be required to undertake unforeseen additional responsibilities or to devote unforeseen additional resources to such development or commercialization, or such development or commercialization could be terminated. Further, termination of an agreement could result in the loss of certain technology rights. Any such event could adversely affect the Company's financial condition, intellectual property position and operations.

The collaborative arrangements that the Company has entered into and may enter into in the future have or may place responsibility for conducting clinical trials, obtaining regulatory approval for potential pharmaceutical products and commercializing such products on the collaborative partner. Should a collaborative partner fail to develop or commercialize successfully any potential product to which it has rights, on a timely basis, the Company's business may be adversely affected. There can be no assurance that the collaborators will not pursue alternative technologies or develop products either on their own or in collaboration with others, as a means for developing treatments for the diseases or disorders targeted by the Company's programs.

Furthermore, the Company has granted to certain of its existing collaborators and expects to grant to future collaborators certain exclusive (even as to the Company) or near exclusive rights to commercialize the Company's



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technology within specified areas, such as the treatment of a particular disease state or condition (e.g., in the case of the Company's agreement with Astra AB, the treatment of pain through encapsulated cell therapy) or the treatment of a particular disease through the use of a particular category of technology (e.g., in the case of the Company's collaboration with Genentech, the use of certain neurotrophic factors in connection with particular diseases). These arrangements make the Company's ability to commercialize its technology in such areas heavily dependent on the performance of such collaborators, prevent the Company from seeking to commercialize its technology in such areas with others and may make it more difficult or impossible for the Company to reach agreement with desirable collaborators in other related or potentially overlapping areas.

NEED FOR AND UNCERTAINTY OF OBTAINING PATENT PROTECTION AND PROPRIETARY RIGHTS

The Company's success will depend in part on its ability to establish, protect and enforce proprietary rights relating to the design, use and manufacture of its proposed products. While the Company has obtained certain patent rights, there can be no assurance that any patent application will mature into an issued patent or that any existing patent or patents which may issue in the future will adequately protect the Company's products and technology.

Patent protection for products such as those the Company proposes to develop is highly uncertain and involves complex factual and evolving legal questions. No assurance can be given that any patents issued or licensed to the Company will not be challenged, invalidated or circumvented, or that the rights granted under such patents will provide competitive advantages to the Company. In addition to patent protection, the Company also relies substantially on trade secrets and proprietary know-how which it seeks to protect, in part, by confidentiality agreements with collaborators, employees and consultants. There can be no assurance that these agreements will not be breached, that the Company would have adequate remedies for any breach, or that the Company's trade secrets will not otherwise become known or independently discovered by competitors.

EXISTENCE OF THIRD PARTY PATENTS AND PROPRIETARY RIGHTS; NEED TO OBTAIN LICENSES

There are pending patent applications or issued patents held by others relating to the Company's proposed products or the technology to be utilized by the Company in the development of its proposed products. If such patents or other patents are determined by the Company or a court to be valid and infringed, the Company may be required to alter its products or processes, pay licensing fees or royalties or cease certain activities. In particular, a third party has informed the Company that it will receive a United States Patent which such third party asserts will claim a method for alleviating chronic pain in humans using implanted cells. The Company is not able to evaluate the scope, validity or enforceability of such third party's alleged patent position until such patent issues, if ever. The Company is also aware of one issued patent claiming certain methods for treating defective, diseased or damaged cells in the mammalian CNS by grafting genetically modified donor cells from the same mammalian species. In addition, each of the neurotrophic factors which the Company is currently investigating for use in its proposed products is the subject of one or more claims in patents or patent applications of third parties, and certain other neurotrophic factors are the subject of third party patent applications. Many of such third parties are developing products using such factors that would be directly competitive with the Company's proposed products. The Company expects that it may need to obtain one or more licenses in order to use such neurotrophic factors in certain of its proposed products. The Company hopes to obtain such licenses through collaborative arrangements or licensing agreements with the parties owning such rights, such as its agreements with Genentech. The Company may also be required to seek licenses in regard to other cell lines, the techniques used in creating or obtaining such cell lines, the materials used in the manufacture of its implants or otherwise. There can be no assurance that the Company will be able to establish collaborative arrangements or obtain licenses to necessary or desirable technology on acceptable terms, if at all, or that the patents underlying any such licenses will be valid and enforceable.

Litigation, arbitration or regulatory proceedings, which could result in substantial cost and uncertainty to the Company, may also be necessary to enforce patent or other intellectual property rights of the Company or to determine the scope and validity of other parties' proprietary rights. If the outcome of any such litigation or proceeding is adverse to the Company, the Company's business could be adversely affected. To determine priority of invention, the Company may be required to participate in interference proceedings declared by the United States Patent and Trademark Office, which could result in substantial cost and uncertainty to the Company.

# GOVERNMENT REGULATION

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The Company's research, preclinical development and clinical trials, as well as the manufacturing and marketing of its potential products, are subject to extensive regulation by governmental authorities in the United States and other countries. Clinical trials and manufacturing of the Company's potential products will be subject to the rigorous testing and approval processes of the FDA and the independent processes of foreign regulatory authorities. The process of obtaining FDA and other required regulatory approvals is lengthy, expensive and uncertain. There can be no assurance that the Company or its collaborators will be able to obtain the necessary approvals to commence or continue clinical testing or to manufacture or market its potential products in anticipated time frames, if at all. Because the Company's proposed products represent a new therapeutic mode which combines certain aspects of biologics, drugs and devices, the regulatory environment is likely to be particularly complex, uncertain and time-consuming.

Moreover, if regulatory approval of a product is granted, such approval may include significant limitations on the indicated uses for which the product may be marketed. Even if regulatory approval is obtained, a marketed product and its manufacturer are subject to continual review, and discovery of previously unknown problems with a product or manufacturer may result in restrictions on such product or manufacturer, including withdrawal of the product from the market. Failure to comply with applicable regulatory requirements may, among other things, result in fines, suspensions of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution. Present or future government regulation may delay or prevent clinical trials and the manufacture or marketing of the Company's potential products. In addition, such regulation may impose costly procedures upon the Company's activities or furnish a competitive advantage to other companies more experienced in regulatory affairs than the Company.

The U.S. Public Health Service has published "Draft Guidelines on Infectious Disease Issues in Xenotransplantation," which propose recommendations to minimize any potential public health associated with xenotransplantation. Xenotransplantation, in this case, is the transplantation of living cells, tissues or organs from a non- human animal source into humans. There have also been several legislative proposals to reform the FDA. If such guidelines and/or proposals are adopted they may result in significant changes in the regulatory environment the Company faces. These changes could (i) result in different, more costly or more time consuming approval requirements for the Company's products, (ii) adversely affect the Company's ability to recruit subjects for clinical trials, (iii) result in the dilution of FDA resources available to review the Company's products, or (iv) result in other unpredictable consequences.

The Company has exported and expects to continue to export certain materials for incorporation by its collaborators in products used in foreign clinical trials. The Company believes its export of these materials has been in compliance with applicable FDA policies. The Company expects to seek FDA approval for exports of finished products for clinical trials. Both the Company's past and future export practices could be subject to FDA challenge and there can be no assurance that the FDA would agree that such practices are in compliance with applicable law and regulations or that such exports would be allowed. If the Company were to be prohibited from exporting materials for use in foreign clinical trials, such trials could be delayed or prevented, which could have an adverse effect on the Company. Proposed regulations of the FDA and other governmental agencies, which would place restrictions on researchers who have a financial interest in the outcome of their research, could limit the ability of the Company to include studies conducted by certain of its collaborators in applications by the Company to the FDA, which could have an adverse effect on the Company to the Company.

The Company is subject to numerous environmental and safety laws and regulations. Any violation of, and the cost of compliance with, these regulations could adversely impact the Company's operations. While the Company believes that its procedures comply with applicable regulatory standards, the risk of accidental contamination or injury cannot be completely eliminated. If such an accident were to occur, the Company could be held liable for any resulting damages, and any such liability could exceed the resources of the Company.

## SOURCES OF CELLS AND OTHER MATERIALS

The Company's potential products require genetically engineered cell lines or living cells harvested from animal or human sources. The selection and growth of living cells for human implantation is a relatively new field. There can be no assurance that the Company will successfully identify or develop sources of the cells required for its potential products and obtain such cells in quantities sufficient to satisfy the requirements of its potential products. These supply



limitations may apply, in particular, to primary cells which must be drawn directly from animal or human sources, such as the bovine adrenal chromaffin cells currently used in the Company's pain product. Moreover, the use of primary cells may entail the risk of infection arising from such cells. There can be no assurance that the Company will be able to commercialize the cells and cell lines used in animal studies or clinical trials to date or that the Company will be successful in identifying and obtaining appropriate cell lines for its research programs and proposed products. Failure to identify and obtain or develop the cells or cell lines required for its potential products would have a material adverse effect on the Company.

As an alternative to primary cells, the Company is developing products based on the use of genetically altered cells. Intellectual property rights to important genetic constructs used in developing such cells, including the constructs used to develop cells producing neurotrophic factors, may be claimed by one or more companies, which could prevent the Company from using such cells.

Concerns about the risks of using certain materials in human implants have caused many suppliers of such materials to restrict their use in patients or to cease manufacturing such materials. The failure to obtain reasonable sources of such materials at reasonable prices, if at all, could have a material adverse effect on the Company.

## MANUFACTURING UNCERTAINTIES

The Company's pilot manufacturing plant, without additional expansion, may not have sufficient capacity to permit the Company to produce all the products for clinical trials it anticipates developing. In addition, the Company has not developed the capability to commercially manufacture any of its proposed products and is unaware of any other company which has manufactured any membrane-encapsulated cell product on a commercial scale. Manufacture of the Company's proposed products is expected to require specialized, automated equipment capable of forming complex polymer membranes into implants which combine media, matrices and living cells, all of which must be carried out on a precisely controlled basis, under sterile conditions in a clean-room environment. Failure to achieve manufacturing capability or to demonstrate consistent results using manufactured prototypes in preclinical animal studies or clinical trials could prevent or delay submission of products for regulatory approval and initiation of new product development programs, which could have a material adverse effect on the Company. There can be no assurance that the Company will be able to develop the capability of manufacturing any of its proposed products at a cost or in the quantities necessary to make a commercially viable product, if at all.

The implants for the Company's preclinical studies and the initial clinical trial have generally been constructed using labor-intensive and time-consuming techniques. There can be no assurance that the Company will be successful in developing an effective and efficient manufacturing capability for any of its products. Even if the Company develops techniques for manufacturing its products, the Company's current facilities and staff are inadequate for commercial scale production of its products under development. The Company will be required to develop manufacturing capabilities on its own or identify and contract with manufacturers to produce its products in commercial quantities. There can be no assurance that the Company can develop such facilities or contract with third party manufacturers on acceptable terms, if at all.

### TECHNOLOGICAL CHANGE AND COMPETITION

The development of human therapeutic products is marked by rapid and significant technological change. The Company expects that the technologies associated with its research and development will continue to develop rapidly, and the Company's future success will depend in large part on its ability to maintain a competitive position with respect to these technologies. Technological development by the Company or others may result in the obsolescence of products or processes before the Company recovers the research, development and commercialization expenses it has incurred. There can be no assurance that the Company will successfully address these technological challenges or others that may arise in the course of development.

Competitors of the Company are numerous and include major pharmaceutical and chemical companies, biotechnology companies, universities and other research institutions. Currently, several of these competitors market and sell therapeutic products for the treatment of chronic pain, Parkinson's disease and other CNS conditions. In addition, most of the Company's competitors have substantially greater capital resources, research and development staffs, facilities, experience in conducting clinical trials and obtaining regulatory approvals and, in the case of

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commercial entities, experience in manufacturing and marketing pharmaceutical products, than the Company. These competitors may now have or in the future develop new technologies or use existing technologies that are or may in the future be the basis for competitive products that are alternative or superior treatments for the diseases or conditions which the Company's products are intended to address. The Company's competitors may possess or obtain patent protection or other intellectual property or other rights that block the Company's ability to develop its potential products or may obtain regulatory approval for commercialization of competitive products earlier than the Company. A number of other companies are attempting to develop methods of delivering therapeutic substances within or across the blood brain barrier. There can be no assurance that the Company's competitors will not succeed in developing technologies and products that are more effective than those being developed by the Company or that would render the Company's technology and products obsolete or non-competitive.

### DEPENDENCE ON KEY PERSONNEL

The Company is highly dependent on the principal members of its management and scientific staff and certain of its outside consultants. Loss of the services of any of these individuals could have a material adverse effect on the Company's operations. The Company has no long-term employment or consulting contracts with any of its employees or consultants and does not maintain key person life insurance on any employee or consultant. In addition, the Company's operations are dependent upon its ability to attract and retain additional qualified scientific and management personnel. There can be no assurance the Company will be able to attract and retain such personnel on acceptable terms given the competition among pharmaceutical, biotechnology and healthcare companies, universities and research institutions for experienced personnel.

#### SALES AND MARKETING UNCERTAINTIES

If the Company is successful in developing and obtaining regulatory approval for its products, it may market and sell its proposed products primarily through co-marketing, licensing or other arrangements with third parties. There can be no assurance that the Company will be successful in entering into such arrangements. The Company currently has no experience in sales, marketing or distribution. To the extent that the Company markets its products directly, the Company must develop a marketing staff and sales force with technical expertise. There can be no assurance that the Company will be able to build such a marketing staff or sales force, that the cost of establishing a marketing staff or sales force will not exceed any product revenues or that the Company's sales and marketing efforts will be successful.

## REIMBURSEMENT AND HEALTHCARE REFORM

In both domestic and foreign markets, sales of the Company's potential products will depend in part upon the availability and amounts of reimbursement from third-party healthcare payor organizations, including government agencies, private healthcare insurers and other healthcare payors such as health maintenance organizations and self-insured employee plans. There is considerable pressure to reduce the cost of therapeutic products. In particular, reimbursement from government agencies and insurers and large health organizations may become more restrictive in the future. The Company's potential products represent a new mode of therapy, and, while the cost-benefit ratio of the products may be favorable, the Company expects that the costs associated with its products will be substantial. There can be no assurance that the Company's proposed products will be considered cost-effective by third party payors, that reimbursement will be available or, if available, that such payors' reimbursement policies will not adversely affect the Company's ability to sell its products on a profitable basis, or at all. There can be no assurance that reimbursement will be provided by such payors at all or without substantial delay, or, if such reimbursement is provided, that the approved reimbursement amounts will provide sufficient funds to enable the Company to become profitable.

The revenues and profitability of healthcare related companies, including the Company, may be affected by the continuing efforts of governmental and third party payors to contain or reduce the cost of healthcare through various means. For example, in certain foreign markets pricing or profitability of prescription pharmaceuticals is subject to government control. In the United States, there have been, and the Company expects that there will continue to be, a number of Federal and state proposals to implement government control over healthcare costs. It is uncertain what legislative proposals will be adopted or what actions Federal, state or private payors for healthcare goods and services may take in response to any healthcare reform proposals or legislation. The Company cannot predict the effect healthcare reforms may have on its business. Any such reforms, as well as the uncertainty the proposal of reforms has engendered, could have a material adverse effect on the Company.



## 12 PRODUCT LIABILITY

Clinical testing, marketing and sale of the Company's products will expose the Company to the risk of liability resulting from the use of such products, including claims resulting from risks associated with the surgical procedures, materials or cells required for use of the Company's products. There can be no assurance that substantial product liability claims will not be asserted against the Company. While the Company has obtained clinical trial insurance in limited amounts and expects to obtain product liability insurance when its products are commercialized, there can be no assurance that adequate insurance coverage for any product liability purpose will be available at any cost, if at all. Even if insurance is obtained there can be no assurance that product liability claims would be covered by such insurance or that such claims would not have a material adverse effect on the business or financial condition of the Company.

### POTENTIAL VOLATILITY OF STOCK PRICE

The market prices of many publicly traded biotechnology companies have been and may continue to be highly volatile. A variety of events, directly and indirectly affecting the Company and the biotechnology industry, such as announcements of technological innovations or new therapeutic products by the Company or its competitors, clinical trial results, legislative developments, government regulations, developments in patent or other proprietary rights, public concern as to the safety of products developed by the Company or others, fluctuations in the Company's operating results and general market conditions may have a significant impact on the market price of the Company's Common Stock. In recent years, the stock markets have experienced extreme price and volume fluctuations, which have particularly affected the stock market prices for many biotechnology companies and which have often been unrelated to the operating performances of those companies. These broad market fluctuations may adversely affect the market price of the Company's Common Stock. Because of the limited trading volume in the Company's Common Stock, the market price of such Common Stock is particularly subject to price fluctuations. This limited volume may also make it difficult for investors to buy or sell larger blocks of Common Stock without price dislocation.

## SHARES ELIGIBLE FOR FUTURE SALE AND DILUTION

Upon the issuance of all of the shares offered hereby, the Company will have approximately 18,694,887 shares of Common Stock outstanding, assuming no exercise of other outstanding warrants or options to purchase Common Stock. Substantially all shares of the Company's outstanding Common Stock are and will remain eligible for immediate resale as a result of having been registered for resale under the Securities Act of 1933, pursuant to the provisions of Rule 144 or otherwise.

The shares of Common Stock issuable upon the exercise of the Warrant will, upon completion of the offering, be immediately issuable upon the exercise of the Warrant. Upon exercise, such shares will be eligible for immediate resale, as well as any additional shares that may become issuable under the adjustment and antidilution provisions of the Warrant. See "Description of Warrants." An additional 1,038,861 shares of Common Stock are immediately issuable upon the exercise of options outstanding on November 30, 1996. The shares of Common Stock issuable upon the exercise of options have been registered under the Securities Act of 1933 and, upon exercise, will be eligible for immediate resale.

Sales of shares of Common Stock by the Company's stockholders could adversely affect the prevailing market price of the Company's Common Stock.

Under the Company's agreements with Genentech relating to ALS and Parkinson's disease, Genentech, under certain circumstances, is obligated to loan a substantial amount of money to the Company in order to provide the Company sufficient funds to pay certain product development expenses for which the Company is responsible under such agreements. At the option of the Company, these loans may be repaid, with interest, in cash or in shares of the Company's Common Stock (based on the market price of the Company's Common Stock at the time the loan is repaid). In the event the Company had insufficient cash to repay such loans or chooses to repay such loans through the issuance of Common Stock, the Company's existing shareholders could experience substantial dilution.

## EFFECT OF CERTAIN CHARTER AND BY-LAW PROVISIONS

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Certain provisions of the Company's Restated Certificate of Incorporation (the "Charter") and By-laws and Delaware law could delay or prevent a change in control of the Company and discourage certain attempts to acquire the Company or to remove incumbent management even if some or a majority of the Company's stockholders deem such an attempt to be in the Company's best interest. These provisions include staggered terms for the Company's Board of Directors, restrictions on the ability of stockholders to act by written consent or to call special meetings of stockholders, limitations on the matters to be considered at special meetings of stockholders and the ability of the Board of Directors to consider factors in addition to the economic benefit to stockholders when evaluating a tender offer or merger or acquisition proposal, as well as the "business combination" provisions of Section 203 of the Delaware General Corporation Law. In addition, the Company's Board of Directors, without further stockholder approval, may issue preferred stock or rights to acquire Common Stock or preferred stock, which could have the effect of delaying, deterring or preventing a change in control of the Company. The issuance of preferred stock could also adversely affect the voting power of the holders of Common Stock. While the Company has no present plans to issue shares of preferred stock, the Company may consider from time to time the issuance of preferred stock in connection with corporate collaborations or other transactions.

## USE OF PROCEEDS

If and when the Warrant is exercised, the proceeds to the Company from the sale of the 434,500 shares of Common Stock issuable upon the exercise of the Warrant at a price of \$8.00 per share will be approximately \$3,476,000. The Company may also receive additional proceeds in the event the holder of the Warrant exercises the Additional Antidilution Rights granted pursuant to the Warrant.

The Company intends to use the net proceeds of this offering to fund research and development activities, including preclinical and clinical testing, related to its proposed products for the treatment of chronic pain, Parkinson's disease, Huntington's disease and ALS and other products; to fund product development and additional research and development activities relating to neurotrophic factors, neural stem cells and further technology development; to provide continued funding for contract research programs; to fund capital expenditures; and for working capital and other general corporate purposes.

The proceeds of this offering may also be used in part to acquire additional rights to technology related to the Company's product development programs, and to fund additional collaborative arrangements with other companies and universities when the Company believes such opportunities would enhance its competitive position or complement the Company's current research programs.

The Company expects to use all of the net proceeds of this offering for the purposes described above and will require substantial additional funds in the future. The amounts and timing of the Company's expenditures for these purposes will depend upon a number of factors, including the progress of the Company's research and development, the scope and results of preclinical studies and clinical trials, the cost and timing of regulatory approvals, the need for and availability of third party patent rights, the rate of technological advances, determinations as to the commercial potential of the Company's products under development, the status of competitive products and the establishment of manufacturing capacity. In addition, expenditures will depend on the establishment of collaborative research arrangements with other companies, the availability of other financing and other factors.

Pending application of the proceeds as described above, the Company intends to invest the net proceeds of this offering primarily in government and investment grade debt securities.

### DILUTION

The net tangible book value of the Company as of September 30, 1996, was \$34,623,082 or \$2.24 per share of Common Stock. "Net tangible book value" per share represents the amount of tangible assets of the Company less total liabilities, divided by the number of shares of Common Stock outstanding. After giving effect to the sale by the Company of the 434,500 shares of Common Stock issuable upon exercise of the Warrant (assuming no exercise of the Additional Antidilution Rights set forth in the Warrant), the pro forma net tangible book value of the Company as of September 30, 1996 would have been \$38,099,082, or \$2.40 per share of Common Stock. This represents an immediate increase in the net tangible book value of \$.16 per share to existing stockholders and an immediate dilution of \$5.60 per share to the holder of the Warrant (assuming the Warrant is exercised in full). The following table illustrates this per share dilution:

Assumed public offering price per share of Common Stock(1) Net tangible book value per share as of September 30, 1996 Increase per share attributable to the Warrant holder (upon exercise of the Warrant)	\$2.24 .16	\$8.00
Pro forma net tangible book value per share after offering		2.40
Dilution per share to the Warrant holder (upon exercise of the Warrant)		\$5.60 =====

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## (1) Before deduction of offering expenses payable by the Company.

The following table summarizes as of September 30, 1996 on a pro forma basis the difference between existing stockholders and the holder of the Warrant with respect to the number of shares purchased from the Company and the total consideration and the average price per share paid (assuming exercise of the Warrant in full at \$8.00 per share):

	SHARES PURCHASED		TOTAL CONSIDERATION		AVERAGE PRICE	
	NUMBER	PERCENT	AMOUNT	PERCENT	PER SHARE	
Existing stockholders	15,423,480	97%	\$111,815,092	97%	\$7.25	
Warrant holder	434,500	3%	3,476,000	3%	8.00	
Total	15,857,980	100%	\$115,291,092	100%		
	=========	====	===========	====		

Excludes shares of Common Stock reserved for issuance upon exercise of the Additional Antidilution Rights granted pursuant to the Warrant and 829,171 shares of Common Stock issued in December 1996 to Genentech, Inc. at a per share price of \$10.01. Also, excludes 2,039,163 shares of Common Stock reserved for issuance pursuant to stock options outstanding on September 30, 1996 at a weighted average exercise price of \$8.17 per share, of which options to purchase 997,541 shares were exercisable. Also excludes 31,545 shares of Common Stock reserved for issuance pursuant to warrants outstanding on September 30, 1996 at a weighted average exercise price of \$6.70 per share, all of which were exercisable. Shares issued pursuant to certain outstanding options awarded under such plans may have a dilutive effect on investors purchasing shares in this offering.

Upon the exercise of Additional Antidilution Rights set forth in the Warrant, the holder of the Warrant may experience additional dilution if the per share purchase price of the shares issuable upon the exercise of the Additional Antidilution Rights is greater than the net tangible book value per share of the Company's Common Stock at the time of such exercise. The following summary of the provisions of the Warrant is qualified in its entirety by reference to the form of Warrant Certificate, a copy of which is filed as an Exhibit to the Registration Statement of which this Prospectus is a part.

### RIGHTS TO PURCHASE COMMON STOCK

The Warrant entitles the holder (the "Warrant Holder") to the right (the "General Warrant Right") to purchase 434,500 shares of Common Stock at a price of \$8.00 per share (subject to adjustment as described below) at any time through April 30, 2000, when the Warrant expires. The holder of the Warrant may exercise all or a portion of the Warrant held by such holder by executing the appropriate subscription form attached to the Warrant Certificate and delivering the form to the Company, together with the payment of the exercise price for the shares of Common Stock purchased. The exercise price may be paid by certified or bank check or by wire transfer. The Warrant may be exercised on more than one occasion prior to expiration of the Warrant.

The Company has authorized and reserved for issuance a number of shares of Common Stock sufficient to provide for the exercise of the right to purchase shares currently represented by the Warrant. When issued against receipt of the payment provided for in the Warrant, each share of Common Stock will be fully paid and non-assessable.

The Warrant holder will not have any voting or other rights as stockholders of the Company.

Redemption Rights. The Warrant may, subject to certain exceptions, be redeemed by the Company at a price of \$.05 each, upon 30 days prior written notice, if the average of the closing sale prices of the Common Stock (as reported by the Nasdaq National Market System) exceeds \$12.00 per share for any thirty (30) consecutive trading days ending within 30 days of the notice of redemption. The General Warrant Rights contained in the Warrant so called for redemption will be forfeited unless such Warrant is exercised prior to the date specified in the notice of redemption.

Transferability. The Warrant is nontransferable and no public market for trading the Warrant is expected to exist.

Adjustments. The exercise price of the Warrant, the number of shares of Common Stock issuable upon the exercise of the General Warrant Rights and the price at which the Company may redeem the Warrant are subject to adjustment in the event of a stock dividend, stock split, reverse stock split, recapitalization, merger, consolidation or certain other events. In the event of the complete liquidation and dissolution of the Company, the Warrant will terminate.

Additional Antidilution Rights. In addition to the foregoing adjustments, each Warrant Holder has the right, in the event the Company issues additional shares of Common Stock or other securities convertible into Common Stock, to purchase, at the then market price for such Common Stock, sufficient additional shares of Common Stock to maintain the Warrant Holder's percentage ownership of the Company's Common Stock at the same percentage as was obtained by the Warrant Holder solely by the purchase of the Common Stock. These rights do not apply in the case of any issuance by the Company under any Stock option, equity incentive, Stock bonus, Stock purchase, employee benefit, profit sharing, 401(k), retirement or similar plan or by the Company in the ordinary course of business in connection with lease or bank financings or consulting arrangements. In addition, these rights do not apply in the case of any issue of shares to a single purchaser to the extent that any of such shares (the "Excluded Shares") represent an increase in the purchaser's ownership of the Company's Common Stock above 30% (giving effect to completion of the issuance and assuming conversion of all securities of the Company convertible into common Stock but not including any shares issuable on the exercise of options or warrants) and all such Excluded Shares shall be excluded in determining the Warrant Holder's percentage ownership of the Company's Common Stock. The additional antidilution rights described in this paragraph apply to any issuance by the Company occurring on or before April 30, 2000 and survive redemption of the warrants. Such additional antidilution rights, however, expire in the event that the Warrant Holder (i) in the case of any issuance giving rise to such rights, fails to fully exercise such rights by purchasing substantially all of the shares of Common Stock which such Warrant Holder is entitled to purchase thereunder or (ii) at any time sells any shares of Common Stock or any other security of the Company which is convertible into shares of Common Stock. Under certain

circumstances, exercise of such rights is subject to the Warrant Holder's prior exercise of such Holder's General Warrant Rights. The Company has registered the sale of 2,000,000 shares of Common Stock issuable on exercise of the additional antidilution rights described in this paragraph under the Registration Statement of which this Prospectus is a part.

## FEDERAL INCOME TAX CONSEQUENCES

No gain or loss will be recognized upon the exercise of a Warrant. The holder's basis in the Common Stock received on exercise of a Warrant will equal the holder's basis in the Warrant plus the amount of the exercise price. The holding period of the Common Stock acquired on exercise of a Warrant will commence on the date of the exercise.

Assuming that the holder of a Warrant is not a dealer in warrants and that the Common Stock would have constituted a capital asset in the hands of the holder had the holder exercised the Warrant, any gain or loss realized on a sale or exchange of a Warrant (including a loss realized due to the failure of a holder to exercise a Warrant prior to its expiration) will generally be treated as a capital gain or capital loss for Federal income tax purposes. Gain or loss will be measured by the difference between the amount realized on the sale, exchange or expiration and the holder's basis in the Warrant.

If the Warrants are redeemed by the Company, the holder of a Warrant will recognize gain or loss equal to the difference between his basis in the Warrant and the redemption price of the Warrant. The Internal Revenue Service has taken the position that the termination of a contractual obligation does not constitute a sale or exchange for Federal income tax purposes. If this position is correct and were applied to a redemption of the Warrants, any gain or loss realized on such a redemption would constitute ordinary income or ordinary loss. If, however, a redemption of a Warrant constitutes a sale or exchange for Federal income tax purposes, and if the Common Stock receivable upon exercise of the Warrant would have been a capital asset in the holder's hands if the Warrant had been exercised, then any gain or loss realized by the holder will be capital gain or loss.

### PLAN OF DISTRIBUTION

The shares of Common Stock offered hereby are being offered for sale directly by the Company upon the exercise of the Warrant and the exercise of certain Additional Antidilution Rights granted pursuant to the Warrant. See "Description of Warrants." The exercise price of the Common Stock underlying the Warrant has been determined through negotiations between the Company and the purchaser of the Warrant.

There can be no assurance that the Company will be successful in selling any or all of the shares of Common Stock offered hereby. The Company has not fixed a minimum number of shares of Common Stock to be sold pursuant to this Prospectus. Therefore, the Company may sell less than all of the shares of Common Stock offered hereby, which may significantly reduce the amount of proceeds to be received by the Company. Funds received by the Company on the sale of less than all of the shares of Common Stock offered hereby will not be placed in an escrow, trust or similar account.

The Chief Executive Officer and Chief Financial Officer of the Company, with the assistance of other officers as needed, will participate in the sale of the shares of Common Stock to the purchasers. These participants, who will not receive any compensation for these activities, will not be deemed to be brokers pursuant to Rule 3a4-1 under the Securities Exchange Act of 1934, as amended. The Company does not expect to offer or sell shares of Common Stock in any state whose securities laws would require that the shares of Common Stock only be sold through licensed brokers or dealers.

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## VALIDITY OF SECURITIES

The legality of the securities offered hereby will be passed upon for the Company by Ropes & Gray, Boston, Massachusetts.

#### EXPERTS

The financial statements of the Company incorporated by reference in the Company's Annual Report (Form 10-K) for the year ended December 31, 1995, have been audited by Ernst & Young LLP, independent auditors, as set forth in their report incorporated by reference therein and incorporated herein by reference. Such financial statements are incorporated herein by reference in reliance upon such report given upon the authority of such firm as experts in accounting and auditing.

## ADDITIONAL INFORMATION

The Company has filed with the Securities and Exchange Commission (the "Commission") a Registration Statement (which term shall include all amendments, exhibits and schedules thereto) on Form S-3 under the Securities Act of 1933, as amended, with respect to the shares of Common Stock offered hereby. This Prospectus does not contain all the information set forth in the Registration Statement, certain parts of which are omitted in accordance with the rules and regulations of the Commission, and to which reference is hereby made. Statements made in this Prospectus as to the contents of any document referred to are not necessarily complete. With respect to each such document filed as an exhibit to the Registration Statement, reference is made to the exhibit for a more complete description of the matter involved, and each such statement shall be deemed qualified in its entirety by such reference. The Registration Statement may be inspected and copied at the public reference facilities maintained by the Commission referred to above in "Available Information."

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NO PERSON HAS BEEN AUTHORIZED TO GIVE ANY INFORMATION OR TO MAKE ANY REPRESENTATIONS IN CONNECTION WITH THIS OFFERING OTHER THAN THOSE CONTAINED IN THIS PROSPECTUS, AND, IF GIVEN OR MADE, SUCH INFORMATION OR REPRESENTATIONS MUST NOT BE RELIED UPON AS HAVING BEEN AUTHORIZED BY THE COMPANY. THIS PROSPECTUS DOES NOT CONSTITUTE AN OFFER TO SELL OR A SOLICITATION OF AN OFFER TO BUY ANY SECURITIES OTHER THAN THE SECURITIES TO WHICH IT RELATES OR AN OFFER TO, OR A SOLICITATION OF, ANY PERSON IN ANY JURISDICTION WHERE SUCH AN OFFER OR SOLICITATION WOULD BE UNLAWFUL. NEITHER THE DELIVERY OF THIS PROSPECTUS NOR ANY SALE MADE HEREUNDER SHALL, UNDER ANY CIRCUMSTANCES, CREATE AN IMPLICATION THAT THERE HAS BEEN NO CHANGE IN THE AFFAIRS OF THE COMPANY SINCE THE DATE HEREOF OR THAT INFORMATION CONTAINED HEREIN IS CORRECT AS OF ANY TIME SUBSEQUENT TO THE DATE HEREOF.

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2,434,500 shares of Common Stock

CytoTherapeutics, Inc.

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## PROSPECTUS

December \_\_\_, 1996

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#### INFORMATION NOT REQUIRED IN PROSPECTUS

## Item 14. Other Expenses of Issuance and Distribution.

Estimated expenses (other than fees and commissions) payable in connection with the sale of the Common Stock offered hereby are as follows\*:

SEC Registration Fee..... 4,828 \$ NASDAQ National Market Additional Listing Fee..... 17,500 Blue Sky Fees and Expenses..... 10,000 Legal Fees and Expenses..... 100,000 Accounting Fees and Expenses..... 30,000 Printing, Engraving and Mailing Expenses..... 40,000 Transfer Agent Fees and Expenses..... 5,000 Miscellaneous..... 17,672

Total.....\$ 225,000

\* Substantially all of these expenses were incurred and paid in connection with offering of certain units of the Company in May 1995 that were registered on this Registration Statement and of which the Warrant was a part.

## Item 15. Indemnification of Directors and Officers.

Section 145 of the Delaware General Corporation Law, as amended (the "DGCL"), provides that a corporation may indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal or investigative (other than an action by or in the right of the corporation) by reason of the fact that he is was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by him in connection with such action, suit or proceeding if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful. Section 145 further provides that a corporation similarly may indemnify any such person serving in any such capacity who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor, against expenses actually and reasonably incurred in connection with the defense or settlement of such action or suit if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation and except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Delaware Court of Chancery or such other court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Section 102(b)(7) of the DGCL permits a corporation to include in its certificate of incorporation a provision eliminating or limiting the personal liability of a director to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, provided that such provision shall not eliminate or limit the liability of a director (i) for any breach of the director's duty of loyalty to the corporation or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the DGCL (relating to unlawful payment of dividends and unlawful stock purchase and redemption) or (iv) for any transaction from which the director derived an improper personal benefit.

The Registrant's Restated Certificate of Incorporation provides that the Registrant's directors shall not be liable to the Registrant or its stockholders for monetary damages for breach of fiduciary duty as a director, except to the extent that exculpation from liabilities is not permitted under the DGCL as in effect at the time such liability is determined. The Restated Certificate of Incorporation further provides that the Registrant shall indemnify its directors and officers to the full extent permitted by the law of the State of Delaware. Item 16. Exhibits and Financial Statement Schedules.

The exhibits listed in the Exhibit Index as filed as part of this Registration Statement.

(a) Exhibits

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Exhibit No	Title or Description
	· · · · · · · · · · · · · · · · · · ·
3.1*	Restated Certificate of Incorporation of the Registrant.
3.2+	Amended and Restated By-laws of the Registrant.
4*	Specimen Common Stock Certificate.
4.1++	Form of Warrant Certificate issued to a certain purchaser of the Registrant's Common Stock in April 1995.
5!	Opinion of Ropes & Gray.
23.1	Consent of Ernst & Young LLP.
23.2!	Consent of Ropes & Gray (included in the opinion filed as Exhibit 5).
24	Power of Attorney (included on signature page).

- \* Previously filed with the Commission as Exhibits to, and incorporated herein by reference to, Registration Statement on Form S-1, File No. 33-45739.
- + Previously filed with the Commission as Exhibits to, and incorporated by reference to, Registration Statement on Form S-1, File No. 33-85494.
- ++ Previously filed with the Commission, as an Exhibit to this Registration Statement on April 14, 1995.
- Previously filed with the Commission on Exhibit to Pre-Effective Amendment No. 1 to this Registration Statement on April 27, 1995.
  - (b) Financial Statement Schedules -- None

All schedules for which provision is made in the applicable accounting regulations of the Securities and Exchange Commission are not required under the related instructions or are inapplicable and, therefore, have been omitted.

#### Item 17. Undertakings.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions described above in Item 15, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes (1) that for purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of the Registration Statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Act shall be deemed to be part of this Registration Statement as of the time it was declared effective; and (2) that for the purpose of determining any liability under the Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered herein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's Annual Report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

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## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, CytoTherapeutics, Inc. certifies that it has reasonable grounds to believe that it meets all the requirements for filing Post-Effective Amendment No. 1 to Form S-1 on Form S-3 (the "Amendment") and has duly caused this Amendment to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Providence, Rhode Island on the 20th day of December, 1996.

CYTOTHERAPEUTICS, INC.

By: /s/ Daniel E. Geffken Daniel E. Geffken Vice President, Chief Financial Officer and Treasurer

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed below by the following persons in the capacities indicated.

Signature	Capacity	Date 
* Seth A. Rudnick, M.D.	Chairman, Chief Executive Officer, and Director (principal executive officer)	December 20, 1996
* Sandra Nusinoff Lehrman, M.D.	President, Chief Operating Officer and Director	December 20, 1996
/s/ Daniel E. Geffken Daniel E. Geffken	Vice President, Chief Financial Officer and Treasurer (principal financial and accounting officer)	December 20, 1996
* Edwin C. Cadman, M.D.	Director	December 20, 1996
* Donald R. Conklin	Director	December 20, 1996
* Mark J. Levin	Director	December 20, 1996
* Richard J. Ramsden	Director	December 20, 1996
/s/ Peter Simon  Peter Simon	Director	December 20, 1996
/s/ Patrick Aebischer Patrick Aebischer, M.D., Ph.D.	Director	December 20, 1996

24 \*By: /s/Daniel E. Geffken Daniel E. Geffken Attorney-In-Fact

We, the undersigned directors and officers of CytoTherapeutics, Inc., hereby severally constitute and appoint Seth A. Rudnick, Daniel E. Geffken, and Frederic A. Eustis, III, and each of them singly, our true and lawful attorneys with full power to them, and each of them singly, to sign for us and in our names in the capacities indicated below, the Registration Statement filed herewith and any and all amendments to said Registration Statement (including other post-effective amendments), and generally to do all such things in our name and behalf in our capacities as officers and directors to enable CytoTherapeutics, Inc. to comply with the provisions of the Securities Act of 1933, and all requirements of the Securities and Exchange Commission, hereby ratifying and confirming our signatures as they may be signed by our said attorneys, or any of them, to said Registration Statement and any and all amendments thereto.

/s/ Patrick Aebischer Director
Patrick Aebischer, M.D., Ph.D.

December 20, 1996

/s/ Peter Simon Peter Simon Director

December 20, 1996

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## EXHIBIT INDEX

Exhibit No	. Title or Description
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- Previously filed with the Commission on Exhibit to Pre-Effective Amendment No. 1 to this Registration Statement on April 27, 1995.

# Consent of Independent Auditors

We consent to the reference to our firm under the caption "Experts" in Amendment No. 1 to Post-Effective Amendment No. 1 to the Registration Statement (Amendment to Form S-1 on Form S-3 No. 33-91228) and related Prospectus of CytoTherapeutics, Inc. for the registration of 2,434,500 shares of its common stock and to the incorporation by reference therein of our report dated January 22, 1996 with respect to the financial statements of CytoTherapeutics, Inc. incorporated by reference in its Annual Report (Form 10-K) for the year ended December 31, 1995, filed with the Securities and Exchange Commission.

ERNST & YOUNG LLP

Boston, Massachusetts December 19, 1996