

[LOGO]

INHALE THERAPEUTIC SYSTEMS, INC.

3,752,456 SHARES OF COMMON STOCK

The selling security holders may sell up to 3,752,456 shares of common stock of Inhale Therapeutic Systems, Inc., a Delaware corporation. The selling security holders may sell the common stock described in this prospectus in a number of different ways and at varying prices. We will not receive any proceeds from the sale of these shares by the selling security holders.

Our common stock currently trades on the Nasdaq National Market under the symbol "INHL". The last reported sale price on January 31, 2001 was \$38.31 per share.

We will not be paying any underwriting commissions or discounts in the offering of these shares.

INVESTING IN OUR COMMON STOCK INVOLVES A HIGH DEGREE OF RISK. PLEASE CAREFULLY CONSIDER THE "RISK FACTORS" BEGINNING ON PAGE 3 OF THIS PROSPECTUS.

-----

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.

-----

In connection with this offering, no person is authorized to give any information or to make any representations not contained in this prospectus. If information is given or representations are made, you may not rely on that information or representations as having been authorized by us. This prospectus is neither an offer to sell nor a solicitation of an offer to buy any securities other than those registered by this prospectus, nor is it an offer to sell or a solicitation of an offer to buy securities where an offer or solicitation would be unlawful. You may not imply from the delivery of this prospectus, nor from any sale made under this prospectus, that our affairs are unchanged since the date of this prospectus or that the information contained in this prospectus is correct as of any time after the date of this prospectus.

-----

The date of this prospectus is February 5, 2001.

## ABOUT OUR BUSINESS

THE FOLLOWING IS A SHORT SUMMARY OF OUR BUSINESS. YOU SHOULD CAREFULLY READ THE "RISK FACTORS" SECTION OF THIS PROSPECTUS AND OUR AMENDED ANNUAL REPORT ON FORM 10-K/A FOR THE YEAR ENDED 1999 FOR MORE INFORMATION ON OUR BUSINESS AND THE RISKS INVOLVED IN INVESTING IN OUR STOCK. IN ADDITION TO THE HISTORICAL INFORMATION CONTAINED IN THIS PROSPECTUS, THIS PROSPECTUS CONTAINS FORWARD-LOOKING STATEMENTS WITHIN THE MEANING OF SECTION 27A OF THE SECURITIES ACT AND SECTION 21E OF THE EXCHANGE ACT THAT INVOLVE RISKS AND UNCERTAINTIES. OUR ACTUAL RESULTS COULD DIFFER MATERIALLY FROM OUR EXPECTATIONS. FACTORS THAT COULD CAUSE OR CONTRIBUTE TO SUCH DIFFERENCES ARE DISCUSSED IN "RISK FACTORS" BEGINNING AT PAGE 3 OF THIS PROSPECTUS AND IN "MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS" AND "BUSINESS" IN OUR AMENDED ANNUAL REPORT.

We are creating a drug delivery system to easily and painlessly deliver a wide range of drugs, including peptides, proteins, and other molecules, by inhalation to the deep lung for treatment of systemic and respiratory diseases. We are using this system principally to enable non-invasive delivery of macromolecule drugs currently administered by injection. Our most advanced program, which is sponsored by Pfizer Inc., is inhaleable insulin. Pfizer commenced dosing for its Phase III human clinical trials in June 1999. In addition to our insulin program with Pfizer, we have development collaborations with Biogen, Inc., Aventis Behring LLC (a division of Aventis S.A.), and Eli Lilly and Co. We also have early stage feasibility and research collaborations with several other companies and have tested eight drugs in human clinical trials.

Currently there are approximately 35 macromolecule drugs marketed in the United States and about 120 other such drugs in human clinical trials. Sales of the top 15 genetically engineered protein drugs (a subset of macromolecule drugs) were estimated at \$15.6 billion worldwide in 1999. Most of these drugs are currently delivered by injection. Injections are undesirable for numerous reasons including patient discomfort, inconvenience and risk of infection. Poor patient acceptance of, and compliance with, injectable therapies can lead to increased incidence of medical complications and higher disease management costs. Alternatives to injection such as oral, transdermal and nasal delivery have to date been shown generally to be commercially unattractive due to low natural bioavailability—the amount of drug absorbed from the delivery site into the bloodstream relative to injection. As an alternative to the invasiveness of injection, we believe a deep lung inhalation delivery system could expand the market for protein drug therapies by increasing patient acceptance and improving compliance and may enable new therapeutic uses of certain macromolecule drugs.

We are creating a proprietary technology platform integrating customized formulation, dry powder processing and packaging with a proprietary inhalation devices to enable efficient, reproducible delivery of macromolecule drugs for systemic and local lung indications. For specific drug products, we formulate and process bulk drugs supplied by collaborative partners into dry powders which are packaged into individual dosing units referred to as blisters. The blisters are designed to be loaded into our device, which patients then activate to inhale the aerosolized drugs. We have developed an inhalation device that is being used several times per day for several months in outpatient trials for insulin. In addition, we have demonstrated room temperature stability of a year or more for a number of macromolecule drugs, and have scaled-up our powder processing and packaging for late stage clinical trials and small scale production for certain drugs.

Our most advanced product is inhaleable insulin for Type 1 and Type 2 diabetes, which is being developed through a collaborative program with Pfizer. Worldwide insulin and insulin delivery systems sales were estimated to be \$3.2 billion in 1998. Data published by Pfizer and clinical investigators from a 190 person Phase IIb human clinical trial using our drug delivery system showed that inhaleable insulin provided statistically equivalent control of diabetes when compared with injectable mealtime insulin for diabetics on insulin, and improved control of diabetes when compared with injectable mealtime insulin for diabetics on insulin, and improved control of diabetes for patients poorly

controlled on oral therapies. The Phase III trials involve approximately 120 clinical sites. In November 1998, Pfizer announced that it entered into a co-development and co-promotion arrangement with Aventis for inhaleable insulin. Pfizer and Aventis have reported plans to invest over 300 million DM (approximately \$134 million) for the construction of a jointly-owned manufacturing facility in Germany for the supply of insulin for pulmonary delivery. This state-of-the-art insulin plant is projected to be the largest of its kind in the world. We will receive royalties on inhaleable insulin products marketed by Pfizer and Aventis as well as revenues for supplying devices and powders.

In a typical collaboration, our partner will provide the drug, fund clinical development and market the resulting commercial product. We will supply the delivery system and receive revenues from powder manufacturing, device supply and royalties from sales of any commercial products. Prior to commercialization, we receive revenues from our partners for research and development funding and progress payments upon achievement of certain developmental milestones.

In addition to Pfizer's sponsorship of our inhaleable insulin program, we have active pulmonary delivery development programs with Biogen for AVONEX-Registered Trademark-, an interferon beta drug used in the treatment of Multiple Sclerosis; Aventis Behring for an alpha-1 antitrypsin proteinase inhibitor being used for the treatment of genetic emphysema; and Lilly for Forteo-TM-, a parathyroid hormone, or PTH 1-34, being developed for the treatment of osteoporosis. These and other ongoing projects in various stages of research, formulation and clinical development have been selected as focus programs by us because we believe our approach may have significant advantages over current therapies. We anticipate that any product that may be developed would be commercialized with a collaborative partner and believe our partnering strategy will enable us to reduce the investment required to develop a large and diversified potential product portfolio.

Our principal executive offices are located at 150 Industrial Road, San Carlos, CA 94070. Our telephone number is (650) 631-3100. We maintain an Internet home page at [www.inhale.com](http://www.inhale.com). The contents of our web page are not a part of this prospectus.

## RISK FACTORS

IN ADDITION TO THE OTHER INFORMATION CONTAINED IN THIS PROSPECTUS, INVESTORS SHOULD CAREFULLY CONSIDER THE FOLLOWING RISK FACTORS IN EVALUATING AN INVESTMENT IN OUR STOCK. THIS PROSPECTUS INCLUDES "FORWARD-LOOKING STATEMENTS" WITHIN THE MEANING OF SECTION 27A OF THE SECURITIES ACT AND SECTION 21E OF THE EXCHANGE ACT. ALL STATEMENTS OTHER THAN STATEMENTS OF HISTORICAL FACT ARE "FORWARD-LOOKING STATEMENTS" FOR PURPOSES OF THESE PROVISIONS, INCLUDING ANY PROJECTIONS OF EARNINGS, REVENUES OR OTHER FINANCIAL ITEMS, ANY STATEMENTS OF THE PLANS AND OBJECTIVES OF MANAGEMENT FOR FUTURE OPERATIONS, ANY STATEMENTS CONCERNING PROPOSED NEW PRODUCTS OR SERVICES, ANY STATEMENTS REGARDING FUTURE ECONOMIC CONDITIONS OR PERFORMANCE AND ANY STATEMENT OF ASSUMPTIONS UNDERLYING ANY OF THE FOREGOING. IN SOME CASES, FORWARD-LOOKING STATEMENTS CAN BE IDENTIFIED BY THE USE OF TERMINOLOGY SUCH AS "MAY", "WILL", "EXPECTS", "PLANS", "ANTICIPATES", "ESTIMATES", "POTENTIAL", OR "CONTINUE" OR THE NEGATIVE THEREOF OR OTHER COMPARABLE TERMINOLOGY. ALTHOUGH WE BELIEVE THAT THE EXPECTATIONS REFLECTED IN THE FORWARD-LOOKING STATEMENTS CONTAINED HEREIN ARE REASONABLE, THERE CAN BE NO ASSURANCE THAT SUCH EXPECTATIONS OR ANY OF THE FORWARD-LOOKING STATEMENTS WILL PROVE TO BE CORRECT AND ACTUAL RESULTS COULD DIFFER MATERIALLY FROM THOSE PROJECTED OR ASSUMED IN THE FORWARD-LOOKING STATEMENTS. OUR FUTURE FINANCIAL CONDITION AND RESULTS OF OPERATIONS, AS WELL AS ANY FORWARD-LOOKING STATEMENTS, ARE SUBJECT TO INHERENT RISKS AND UNCERTAINTIES, INCLUDING BUT NOT LIMITED TO THE RISK FACTORS SET FORTH BELOW AND FOR THE REASONS DESCRIBED ELSEWHERE IN THIS PROSPECTUS. ALL FORWARD-LOOKING STATEMENTS AND REASONS WHY RESULTS MAY DIFFER INCLUDED IN THIS PROSPECTUS ARE MADE AS OF THE DATE HEREOF AND WE ASSUME NO OBLIGATION TO UPDATE ANY SUCH FORWARD-LOOKING STATEMENT OR REASON WHY ACTUAL RESULTS MIGHT DIFFER.

WE DO NOT KNOW IF OUR DEEP LUNG DRUG DELIVERY SYSTEM IS COMMERCIALY FEASIBLE.

We are in an early stage of development. There is a risk that our deep lung drug delivery technology will not be commercially feasible. Even if our deep lung delivery technology is commercially feasible, it may not be commercially accepted across a range of large and small molecule drugs. We have tested eight deep lung delivery formulations in humans, but many of our potential formulations have not been tested in humans.

Many of the underlying drug compounds contained in our deep lung formulations have been tested in humans by other companies using alternative delivery routes. Our potential products require extensive research, development and preclinical (animal) and clinical (human) testing. Our potential products also may involve lengthy regulatory review before they can be sold. We do not know if, and cannot assure you that any of our potential products will prove to be safe and effective or meet regulatory standards. There is a risk that any of our potential products will not be able to be produced in commercial quantities at acceptable cost or marketed successfully. Our failure to achieve commercial feasibility, demonstrate safety, achieve clinical efficacy, obtain regulatory approval or, together with partners, successfully market products will negatively impact our revenues and results of operations.

WE DO NOT KNOW IF OUR DEEP LUNG DRUG DELIVERY SYSTEM IS EFFICIENT.

We may not be able to achieve the total system efficiency needed to be competitive with alternative routes of delivery. Total system efficiency is determined by the amount of drug loss during manufacture, in the delivery device, in reaching the site of absorption, and during absorption from that site into the bloodstream. Deep lung bioavailability is the percentage of a drug that is absorbed into the bloodstream when that drug is delivered directly to the lungs as compared to injection. Bioavailability is the initial screen for whether deep lung delivery of any systemic drug is commercially feasible. We would not consider a drug to be a good candidate for development and commercialization if its drug loss is excessive at any one stage or cumulatively in the manufacturing and delivery process or if its deep lung bioavailability is too low.

WE DO NOT KNOW IF OUR DEEP LUNG DRUG FORMULATIONS ARE STABLE.

We may not be able to identify and produce powdered versions of drugs that retain the physical and chemical properties needed to work with our delivery device. Formulation stability is the physical and chemical stability of the drug over time and under various storage, shipping and usage conditions. Formulation stability will vary with each deep lung formulation and the type and amount of ingredients that are used in the formulation. Problems with powdered drug stability would negatively impact our ability to develop and market our potential products or obtain regulatory approval.

WE DO NOT KNOW IF OUR DEEP LUNG DRUG DELIVERY SYSTEM IS SAFE.

We may not be able to prove potential products to be safe. Our products require lengthy laboratory, animal and human testing. Most of our products are in preclinical testing or the early stage of human testing. If we find that any product is not safe, we will not be able to commercialize the product. The safety of our deep lung formulations will vary with each drug and the ingredients used in its formulation.

WE DO NOT KNOW IF OUR DEEP LUNG DRUG DELIVERY SYSTEM PROVIDES CONSISTENT DOSES OF MEDICINE.

We may not be able to provide reproducible dosages of stable formulations sufficient to achieve clinical or commercial success. Reproducible dosing is the ability to deliver a consistent and predictable amount of drug into the bloodstream over time both for a single patient and across patient groups. Reproducible dosing requires the development of:

- an inhalation device that consistently delivers predictable amounts of dry powder formulations to the deep lung;
- accurate unit dose packaging of dry powder formulations; and
- moisture resistant packaging.

We may not be able to develop reproducible dosing of any potential product. The failure to do so means that we would not consider it a good candidate for development and commercialization.

WE DEPEND ON PARTNERS FOR REGULATORY APPROVALS AND COMMERCIALIZATION OF OUR PRODUCTS.

Because we are in the business of developing technology for delivering drugs to the lungs and licensing this technology to companies that make and sell drugs, we do not have the people and other resources to do the following things:

- make bulk drugs to be used as medicines;
- design and carry out large scale clinical studies;
- prepare and file documents necessary to obtain government approval to sell a given drug product; and
- market and sell our products when and if they are approved.

When we sign a collaborative development agreement or license agreement to develop a product with a drug company, the drug company agrees to do some or all of the things described above. If our partner fails to do any of these things, we cannot complete the development of the product.

WE MAY NOT OBTAIN REGULATORY APPROVAL FOR OUR PRODUCTS ON A TIMELY BASIS, OR AT ALL.

There is a risk that we will not obtain regulatory approval for our products on a timely basis, or at all. Our product must undergo rigorous laboratory animal and human testing and an extensive review process mandated by the United States Food and Drug Administration ("FDA") and equivalent foreign

authorities. This process generally takes a number of years and requires the expenditure of substantial resources although the time required for completing such testing and obtaining such approvals is uncertain. We have not submitted any of our products to the FDA for marketing approval. We have no experience obtaining such regulatory approval.

In addition, we may encounter delays or rejections based upon changes in FDA policy, including policy relating to good manufacturing practice compliance, or "cGMP", during the period of product development. We may encounter similar delays in other countries.

Even if regulatory approval of a product is granted, the approval may limit the indicated uses for which we may market our product. In addition, our marketed product, our manufacturing facilities and Inhale, as the manufacturer, will be subject to continual review and periodic inspections. Later discovery from such review and inspection of previously unknown problems may result in restrictions on our product or on us, including withdrawal of our product from the market. The failure to obtain timely regulatory approval of our products, any product marketing limitations or a product withdrawal would negatively impact our revenues and results of operations.

WE DO NOT KNOW IF OUR TECHNOLOGIES CAN BE INTEGRATED SUCCESSFULLY TO BRING PRODUCTS TO MARKET.

We may not be able to integrate all of the relevant technologies to provide a deep lung drug delivery system. Our integrated approach to systems development relies upon several different but related technologies:

- dry powder formulations;
- dry powder processing technology;
- dry powder packaging technology; and
- a deep lung delivery device.

At the same time, we must:

- establish collaborations with partners;
- perform laboratory and clinical testing of potential products; and
- scale-up our manufacturing processes.

We must accomplish all of these steps without delaying any aspect of technology development. Any delay in one component of our products or business development activities could delay our ability to develop, obtain approval of or market therapeutic products using our deep lung delivery technology.

WE MAY NOT BE ABLE TO MANUFACTURE OUR PRODUCTS IN COMMERCIAL QUANTITIES.

POWDER PROCESSING. We have no experience manufacturing products for commercial purposes. We have only performed powder processing on the small scale needed for testing formulations and for early stage and larger clinical trials. We may encounter manufacturing and control problems as we attempt to scale-up powder processing facilities. We may not be able to achieve such scale-up in a timely manner or at a commercially reasonable cost, if at all. Our failure to solve any of these problems could delay or prevent late stage clinical testing and commercialization of our products and could negatively impact our revenues and results of operations.

To date, we have relied primarily on one particular method of powder processing. There is a risk that this technology will not work with all drugs or that the cost of drug production will preclude the commercial viability of certain drugs. Additionally, there is a risk that any alternative powder processing methods we may pursue will not be commercially practical for aerosol drugs or that we will not have, or be able to acquire the rights to use, such alternative methods.

POWDER PACKAGING. Our fine particle powders and small quantity packaging require special handling. We have designed and qualified automated filling equipment for small and moderate quantity packaging of fine powders. We face significant technical challenges in scaling-up an automated filling system that can handle the small dose and particle sizes of our powders in commercial quantities. There is a risk that we will not be able to scale-up our automated filling equipment in a timely manner or at commercially reasonable costs. Any failure or delay in such scale-up would delay product development or bar commercialization of our products and would negatively impact our revenues and results of operations.

INHALATION DEVICES. We face many technical challenges in further developing our inhalation devices to work with a broad range of drugs, to produce such devices in sufficient quantities and to adapt the devices to different powder formulations. There is a risk that we will not successfully achieve any of these things. Our failure to overcome any of these things would negatively impact our revenues and results of operations.

For late stage clinical trials and initial commercial production, we intend to use one or more contract manufacturers to produce our drug delivery devices. There is a risk that we will not be able to enter into or maintain arrangements with potential contract manufacturers or effectively scale-up production of our drug delivery devices through contract manufacturers that we identify. Our failure to do so would negatively impact our revenues and results of operations.

WE DEPEND ON SOLE OR EXCLUSIVE SUPPLIERS FOR OUR INHALATION DEVICES AND BULK DRUGS.

We plan to subcontract the manufacture of our pulmonary delivery devices before commercial production of our first products. We have identified contract manufacturers that we believe have the technical capabilities and production capacity to manufacture our devices and which can meet the requirements of good manufacturing practices. We cannot be assured that we will be able to obtain and maintain satisfactory contract manufacturing on commercially acceptable terms, if at all. Our dependence on third parties for the manufacture of our inhalation device may negatively impact our cost of goods and our ability to develop and commercialize products on a timely and competitive basis.

We obtain the bulk drugs we use to formulate and manufacture the dry powders for our deep lung delivery systems from sole or exclusive sources of supply. For example, with respect to our source of bulk insulin, we have entered into a collaborative agreement with Pfizer which has, in turn, entered into an agreement with Aventis to manufacture biosynthetic recombinant insulin. Under the terms of their agreement, Pfizer and Aventis agreed to construct a jointly owned manufacturing plant in Frankfurt, Germany. Until its completion, Pfizer will provide us with insulin from Aventis's existing plant. If our sole or exclusive source suppliers fail to provide bulk drugs in sufficient quantities when required, our revenues and results of operations will be negatively impacted.

WE DO NOT KNOW IF THE MARKET WILL ACCEPT OUR DEEP LUNG DRUG DELIVERY SYSTEM.

The commercial success of our potential products depends upon market acceptance by health care providers, third-party payors like health insurance companies and Medicare, and patients. Our products under development use a new method of drug delivery and there is a risk that our potential products will not be accepted by the market. Market acceptance will depend on many factors, including:

- the safety and efficacy results of our clinical trials;
- favorable regulatory approval and product labeling;
- the frequency of product use;
- the availability of third-party reimbursement;
- the availability of alternative technologies; and

- the price of our products relative to alternative technologies.

There is a risk that health care providers, patients or third-party payors will not accept our deep lung drug delivery system. If the market does not accept our potential products, our revenues and results of operations would be significantly and negatively impacted.

IF OUR PRODUCTS ARE NOT COST EFFECTIVE, GOVERNMENT AND PRIVATE INSURANCE PLANS WILL NOT PAY FOR OUR PRODUCTS.

In both domestic and foreign markets, sales of our products under development will depend in part upon the availability of reimbursement from third-party payors, such as government health administration authorities, managed care providers, private health insurers and other organizations. In addition, such third-party payors are increasingly challenging the price and cost effectiveness of medical products and services. Significant uncertainty exists as to the reimbursement status of newly approved health care products. Legislation and regulations affecting the pricing of pharmaceuticals may change before our proposed products are approved for marketing. Adoption of such legislation and regulations could further limit reimbursement for medical products. A government or third-party payor decision to not provide adequate coverage and reimbursements for our products would limit market acceptance of such products.

WE EXPECT TO CONTINUE TO LOSE MONEY FOR THE NEXT SEVERAL YEARS.

We have never been profitable and, through September 30, 2000, have incurred a cumulative deficit of approximately \$152.3 million. We expect to continue to incur substantial and increasing losses over at least the next several years as we expand our research and development efforts, testing activities and manufacturing operations, and as we further expand our late stage clinical and early commercial production facility. All of our potential products are in research or in the early stages of development except for our insulin collaboration. We have generated no revenues from approved product sales. Our revenues to date have consisted primarily of payments under short-term research and feasibility agreements and development contracts. To achieve and sustain profitable operations, we must, alone or with others, successfully develop, obtain regulatory approval for, manufacture, introduce, market and sell products using our deep lung drug delivery system. There is a risk that we will not generate sufficient product or contract research revenue to become profitable or to sustain profitability.

WE MAY NEED TO RAISE ADDITIONAL CAPITAL THAT MAY NOT BE AVAILABLE.

We anticipate that our existing capital resources will enable us to maintain currently planned operations through at least the next 34 months. However, this expectation is based on our current operating plan, which is expected to change as a result of many factors, and we may need additional funding sooner than anticipated. In addition, we may choose to raise additional capital due to market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of such securities could result in dilution to our stockholders.

We have no credit facility or other committed sources of capital. To the extent operating and capital resources are insufficient to meet future requirements, we will have to raise additional funds to continue the development and commercialization of our technologies. Such funds may not be available on favorable terms, or at all. In particular, our substantial leverage may limit our ability to obtain additional financing. If adequate funds are not available on reasonable terms, we may be required to curtail operations significantly or to obtain funds by entering into financing, supply or collaboration agreements on unattractive terms. Our inability to raise capital could negatively impact our business.

IF WE FAIL TO MANAGE OUR GROWTH EFFECTIVELY, OUR BUSINESS MAY SUFFER.

Our ability to commercialize our products, achieve our expansion objectives, manage our growth effectively and satisfy our commitments under our collaboration agreements depends on a variety of factors. Key factors include our ability to develop products internally, enter into strategic partnerships with collaborators, attract and retain skilled employees and effectively expand our internal organization to accommodate anticipated growth including integration of any potential businesses that we may acquire. If we are unable to manage growth effectively, there could be a material adverse effect on our business, financial condition and results of operations.

OUR PATENTS MAY NOT PROTECT OUR PRODUCTS AND OUR PRODUCTS MAY INFRINGE ON THIRD-PARTY PATENT RIGHTS.

We have filed patent applications covering certain aspects of our device, powder processing technology, and powder formulations and deep lung route of delivery for certain molecules, and we plan to file additional patent applications. We currently have 100 issued U.S. and foreign patents that cover certain aspects of our technology and we have a number of patent applications pending. There is a risk that any of the patents applied for will not issue, or that any patents that issue or have issued will not be valid and enforceable. Enforcing our patent rights would be time consuming and costly.

Our access or our partners' access to the drugs to be formulated will affect our ability to develop and commercialize our technology. Many drugs, including powder formulations of certain drugs that are presently under development by us, are subject to issued and pending U.S. and foreign patents that may be owned by our competitors. We know that there are issued patents and pending patent applications relating to the deep lung delivery of large molecule drugs, including several for which we are developing deep lung delivery formulations. This situation is highly complex, and the ability of any one company, including Inhale, to commercialize a particular drug is unpredictable.

We intend generally to rely on the ability of our partners to provide access to the drugs that are to be formulated by us for deep lung delivery. There is a risk that our partners will not be able to provide access to such drug candidates. Even if such access is provided, there is a risk that our partners or we will be accused of, or determined to be, infringing a third-party's patent rights and will be prohibited from working with the drug or be found liable for damages that may not be subject to indemnification. Any such restriction on access to drug candidates or liability for damages would negatively impact our revenues and results of operations.

OUR COMPETITORS MAY DEVELOP AND SELL BETTER DRUG DELIVERY SYSTEMS.

We are aware of other companies engaged in developing and commercializing pulmonary drug delivery systems, including enhanced injectable and other drug delivery systems. Many of these companies have greater research and development capabilities, experience, manufacturing, marketing, financial and managerial resources than we do and represent significant competition for us. Acquisitions of or collaborations with competing drug delivery companies by large pharmaceutical companies could enhance our competitors' financial, marketing and other resources. Accordingly, our competitors may succeed in developing competing technologies, obtaining regulatory approval for products or gaining market acceptance before us. Developments by others could make our products or technologies uncompetitive or obsolete. Our competitors may introduce products or processes competitive with or superior to ours.

INVESTORS SHOULD BE AWARE OF INDUSTRY-WIDE RISKS.

In addition to the risks associated specifically with Inhale described above, investors should also be aware of general risks associated with drug development and the pharmaceutical industry. These include, but are not limited to:

- changes in and compliance with government regulations;

- handling of hazardous materials;
- hiring and retaining qualified people; and
- insuring against product liability claims.

WE EXPECT OUR STOCK PRICE TO REMAIN VOLATILE.

Our stock price is volatile. In the twelve-month period ending January 31, 2001, based on closing prices on the Nasdaq National Market, our stock price ranged from \$23.156 to \$63.313. We expect it to remain volatile. A variety of factors may have a significant effect on the market price of our common stock, including:

- fluctuations in our operating results;
- announcements of technological innovations or new therapeutic products;
- announcement or termination of collaborative relationships by Inhale or our competitors;
- governmental regulation;
- clinical trial results or product development delays;
- developments in patent or other proprietary rights;
- public concern as to the safety of drug formulations developed by Inhale or others; and
- general market conditions.

Any litigation brought against us as a result of this volatility could result in substantial costs and a diversion of our management's attention and resources, which could negatively impact our financial condition, revenues and results of operations.

OUR SUBSTANTIAL INDEBTEDNESS HAS INCREASED SUBSTANTIALLY AND MAY RESULT IN FUTURE LIQUIDITY PROBLEMS.

As of September 30, 2000, we had approximately \$242.6 million in long-term debt. In October 2000, we entered into a build-to-suit lease transaction, where the estimated present value of minimum lease payments approximates \$46.2 million. Additionally, subsequent to Inhale's quarter ending September 30, 2000, the Company entered into privately negotiated agreements with certain holders of its outstanding 5.0% convertible subordinated notes due February 2007 providing for the conversion of their notes into shares of common stock in exchange for a cash payment. Approximately \$168.6 million aggregate principal amount of such outstanding notes was converted into approximately 4.4 million shares of common stock for cash payments of approximately \$25.5 million. The October 2000 issuance of the 3.5% convertible subordinated notes due 2007 increased our long-term debt by approximately \$230.0 million. This additional indebtedness has and will continue to impact us by:

- increasing our interest expense and related debt service costs;
- making it more difficult to obtain additional financing; and
- constraining our ability to react quickly in an unfavorable economic climate.

Currently, we are not generating sufficient cash flow from operations to satisfy the annual debt service payments that will be required as a result of the sale of the notes. This may require us to use a portion of the proceeds from the sale of the notes to pay interest or borrow additional funds or sell additional equity to meet our debt service obligations. If we are unable to satisfy our debt service requirements, substantial liquidity problems could result, which would negatively impact our future prospects.

## WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 to register the common stock offered by this prospectus. However, this prospectus does not contain all of the information contained in the registration statement and the exhibits and schedules to the registration statement. We strongly encourage you to carefully read the registration statement and the exhibits and schedules to the registration statement. We also file annual, quarterly and special reports, proxy statements and other information with the SEC.

You may inspect and copy such material at the public reference facilities maintained by the SEC at Room 1024, 450 Fifth Street, N.W., Washington, D.C. 20549, as well as at the SEC's regional offices at 500 West Madison Street, Suite 1400, Chicago, Illinois 60661 and 7 World Trade Center, Suite 1300, New York, New York 10048. You may also obtain copies of such material from the SEC at prescribed rates by writing to the Public Reference Section of the SEC, 450 Fifth Street, N.W., Washington, D.C. 20549.

Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. Our SEC filings are also available to the public from the SEC's Website at [www.sec.gov](http://www.sec.gov).

## INCORPORATION BY REFERENCE

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

1. Our Annual Report on Form 10-K for the fiscal year ended December 31, 1999, filed on March 10, 2000, including all material incorporated by reference therein;
2. Our Amendment to Annual Report on Form 10-K/A for the fiscal year ended December 31, 1999, filed on March 14, 2000, including all material incorporated by reference therein;
3. Our Amendment to Annual Report on Form 10-K/A for the fiscal year ended December 31, 1999, filed on April 28, 2000, including all material incorporated by reference therein;
4. Our Definitive Proxy on Schedule 14A, filed on May 3, 2000;
5. Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2000, filed on May 11, 2000, including all material incorporated by reference therein;
6. Our Amendment to Quarterly Report on Form 10-Q/A for the quarter ended March 31, 2000, filed on May 15, 2000, including all material incorporated by reference therein;
7. Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2000, filed August 14, 2000, including all material incorporated by reference therein;
8. Our Quarterly Report on Form 10-Q for the quarter ended September 30, 2000, filed November 14, 2000, including all material incorporated therein;
9. Our Current Report on Form 8-K, filed on February 1, 2000;
10. Our Current Report on Form 8-K, filed on February 9, 2000;
11. Our Current Report on Form 8-K, filed on February 24, 2000;

12. Our Current Report on Form 8-K, filed on September 6, 2000;
13. Our Current Report on Form 8-K, filed on October 10, 2000;
14. Our Current Report on Form 8-K, filed on October 10, 2000;
15. Our Current Report on Form 8-K, filed on October 13, 2000;
16. Our Current Report on Form 8-K, filed on October 30, 2000;
17. Our Current Report on Form 8-K, filed on December 21, 2000;
18. Our Current Report on Form 8-K, filed on January 11, 2001;
19. All other reports filed by us pursuant to Section 13(a) or 15(d) of the Exchange Act since December 31, 1999, including all materials incorporated by reference therein; and
20. The description of the common stock contained in our Registration Statement on Form 8-A.

You may request a copy of these filings, at no cost to you, by writing or telephoning us at: Inhale Therapeutic Systems, Inc. Attention: Investor Relations, 150 Industrial Road, San Carlos, CA 94070 Telephone (650) 631-3100.

Our common stock is quoted on the Nasdaq National Market under the symbol "INHL". The last reported sales price of the common stock on the Nasdaq National Market ("Nasdaq") on January 31, 2001 was \$38.31 per share. You may inspect reports and other information concerning us at the offices of the National Association of Securities Dealers, Inc., 1735 K Street, N.W., Washington, D.C. 20006.

You should rely only on the information incorporated by reference or provided in this prospectus. We have authorized no one to provide you with different information. This prospectus is an offer to sell or to buy only the securities referred to herein, and only under circumstances and in jurisdictions where it is lawful to do so. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front of the document.

#### USE OF PROCEEDS

We will not receive any proceeds from the sale of the shares of common stock offered hereby. See "Selling Security Holders".

SELLING SECURITY HOLDERS

In connection with our acquisition of Bradford Particle Design plc completed in January 2001, we issued to all of the selling shareholders shares of our common stock, and we agreed to register these shares of common stock for resale. This Registration Statement may be suspended if Inhale determines, in good faith, that it is in the best interest of Inhale and its shareholders to defer disclosure of non-public information until such information has reached a more advanced state. During a period of suspension sales under this Registration Statement will be suspended. After two years the potential constraints on tradeability imposed by the Registration Statement referred to above cease to apply. Our registration of the shares of common stock does not necessarily mean the selling shareholders will sell all or any of the shares.

The following table sets forth information known to us with respect to the number of shares of our common stock beneficially owned as of January 30, 2001 by each selling shareholder.

The information provided in the table below with respect to each selling shareholder has been obtained from that selling shareholder. Except as otherwise disclosed below, none of the selling shareholders has, or within the past three years has had, any position, office or other material relationship with us. Because the selling shareholders may sell all or some portion of the shares of common stock beneficially owned by them, we cannot estimate either the number or percentage of shares of common stock that will be beneficially owned by the selling shareholders after this offering. In addition, the selling shareholders may have sold, transferred or otherwise disposed of, or may sell, transfer or otherwise dispose of, at any time or from time to time since the date on which they provided the information regarding the shares of common stock beneficially owned by them, all or a portion of the shares of common stock beneficially owned by them in transactions exempt from the registration requirements of the Securities Act of 1933.

The number of shares beneficially owned by each selling shareholder is determined under Rule 13d-3 promulgated by the SEC under the Securities Exchange Act of 1934, as amended, and the information is not necessarily indicative of beneficial ownership for any other purpose. Except as indicated, and subject to community property laws where applicable and the limitations discussed in this "Selling Shareholders" section, the persons named have sole voting and investment power with respect to all shares shown as beneficially owned by them. Percentage of beneficial ownership is based on 51,411,348 shares of common stock outstanding as of January 30, 2001.

| NAME                                  | SHARES BENEFICIALLY OWNED PRIOR TO OFFERING(1) |         | SHARES BEING OFFERED | SHARES BENEFICIALLY OWNED AFTER OFFERING |         |
|---------------------------------------|--|---------|----------------------|--|---------|
|                                       | NUMBER   | PERCENT |                      | NUMBER                                   | PERCENT |
| Ceredig Owen Humphreys.....           | 10,094   | *       | 10,094               | --                                       | --      |
| Robert David Bigland.....             | 6,143  | *       | 6,143                | --                                       | --      |
| Charles Jefferis Woodburn Benson..... | 14,316   | *       | 14,316               | --                                       | --      |
| Donald Charles Macpherson.....        | 36,702   | *       | 36,702               | --                                       | --      |
| John Anthony Clamp.....               | 4,496  | *       | 4,496                | --                                       | --      |
| Henry Alun Humphreys.....             | 6,790  | *       | 6,790                | --                                       | --      |
| Bridgett Bernadette Humphreys.....    | 6,790  | *       | 6,790                | --                                       | --      |
| Claire Louise Humphreys.....          | 1,468  | *       | 1,468                | --                                       | --      |
| Elen Siobhain Humphreys.....          | 1,468  | *       | 1,468                | --                                       | --      |
| Sir Christopher John Benson.....      | 43,109   | *       | 36,708               | --                                       | --      |
| Mark Antony Loveday.....              | 7,341  | *       | 7,341                | --                                       | --      |
| Ulric David Barnett.....              | 7,341  | *       | 7,341                | --                                       | --      |
| David Lionel Mayhew.....              | 7,341  | *       | 7,341                | --                                       | --      |
| Duncan Robert Hunter.....             | 7,341  | *       | 7,341                | --                                       | --      |

| NAME  | SHARES BENEFICIALLY OWNED PRIOR TO OFFERING(1) |         | SHARES BEING OFFERED | SHARES BENEFICIALLY OWNED AFTER OFFERING |         |
|---|--|---------|----------------------|--|---------|
|   | NUMBER   | PERCENT |                      | NUMBER                                   | PERCENT |
| David Michael Wentworth-Stanley.....          | 7,341  | *       | 7,341                | --                                       | --      |
| Charles Julian Cazalet.....                   | 8,718  | *       | 8,718                | --                                       | --      |
| Anthony David Brampton.....                   | 2,083  | *       | 2,083                | --                                       | --      |
| Tessa Kilgour.....                            | 5,506  | *       | 5,506                | --                                       | --      |
| Robert Darnton Wade.....                      | 6,143  | *       | 6,143                | --                                       | --      |
| Jonathan D. Wade.....                         | 1,035  | *       | 1,035                | --                                       | --      |
| Desmond de Silva, QC.....                     | 1,376  | *       | 1,376                | --                                       | --      |
| Patrick Cantrill.....                         | 917  | *       | 917                  | --                                       | --      |
| Jennifer Clare Cazalet.....                   | 1,376  | *       | 1,376                | --                                       | --      |
| Pinnacle Trustees Ltd a/c Sitova (Chown)..... | 1,835  | *       | 1,835                | --                                       | --      |
| Robert Morton Craven.....                     | 1,284  | *       | 1,284                | --                                       | --      |
| Alexandra Norma Craven.....                   | 1,284  | *       | 1,284                | --                                       | --      |
| Ian M. Gilbert.....                           | 3,206  | *       | 3,206                | --                                       | --      |
| Simon T. Concannon.....                       | 1,376  | *       | 1,376                | --                                       | --      |
| Kenneth Simmonds.....                         | 11,012   | *       | 11,012               | --                                       | --      |
| Carole Julia Nicholson.....                   | 15,678   | *       | 10,214               | --                                       | --      |
| Michael J. Walker.....                        | 917  | *       | 917                  | --                                       | --      |
| Julian Christopher Woodburn Benson.....       | 15,397   | *       | 15,397               | --                                       | --      |
| H. Roger Edmunds.....                         | 1,835  | *       | 1,835                | --                                       | --      |
| John Richard Precious.....                    | 6,423  | *       | 6,423                | --                                       | --      |
| Andreas Saesseli.....                         | 13,323   | *       | 13,323               | --                                       | --      |
| Joseph F. Bohan.....                          | 18,798   | *       | 9,177                | --                                       | --      |
| John Davies.....                              | 27,531   | *       | 27,531               | --                                       | --      |
| Gwyn Humphreys.....                           | 815,130  | 1.59%   | 811,246              | --                                       | --      |
| Peter York.....                               | 815,130  | 1.59    | 811,246              | --                                       | --      |
| Mazen Hanna.....                              | 815,130  | 1.59    | 811,246              | --                                       | --      |
| University of Bradford.....                   | 686,439  | 1.34    | 686,439              | --                                       | --      |
| Walker Morris Trustees Ltd.....               | 18   | *       | 18                   | --                                       | --      |
| 3i Group plc.....                             | 311,085  | *       | 311,085              | --                                       | --      |
| Raymond Botterell.....                        | 4,588  | *       | 4,588                | --                                       | --      |
| Dr. Stephen E. Walker.....                    | 10,303   | *       | 4,588                | --                                       | --      |
| Avril Walker.....                             | 4,588  | *       | 4,588                | --                                       | --      |
| Vincent Brophy.....                           | 4,588  | *       | 4,588                | --                                       | --      |
| David John Mathiesan Ray.....                 | 4,588  | *       | 4,588                | --                                       | --      |
| Derek Pearce.....                             | 4,588  | *       | 4,588                | --                                       | --      |

(1) Shares not being offered include shares issuable upon exercise of outstanding options.

\* Represents beneficial ownership of less than one percent (1%).

None of the selling holders nor any of their affiliates, officers, directors or principal equity holders has held any position or office or has had any material relationship with us within the past three years, although the selling holders may hold additional securities of Inhale. The selling holders acquired the common stock from us in a private transaction on January 8, 2001. All of the shares of common stock purchased by the selling security holders were "restricted securities" under the Securities Act prior to this registration.

## PLAN OF DISTRIBUTION

The selling security holders and their successors, including their transferees, pledgees or donees or their successors, may sell the shares of common stock directly to purchasers or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions from the selling holders or the purchasers. These discounts, concessions or commissions as to any particular underwriter, broker-dealer or agent may be in excess of those customary in the types of transactions involved.

The shares offered hereunder may be sold from time to time by the selling security holders in one or more transactions at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market prices, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions:

- on any national securities exchange or U.S. inter-dealer system of a registered national securities association on which the common stock may be listed or quoted at the time of sale;
- in the over-the-counter market;
- in private transactions;
- by pledge to secure debts and other obligations; or
- a combination of any of the above transactions.

Under the Securities Exchange Act, any person engaged in the distribution of the shares may not simultaneously engage in market making activities with respect to our common stock for a period of two business days prior to the commencement of such distribution. In addition, the selling security holders will be subject to the applicable provisions of the Securities Exchange Act, which provisions may limit the timing of purchases and sales of shares of common stock by the selling security holders or any other such persons.

In order to comply with the securities laws of some jurisdictions, if applicable, the shares of common stock must be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in certain jurisdictions, the shares of common stock may not be sold unless they have been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

The selling security holders and any underwriters, broker-dealers or agents that participate in the sale or distribution of the shares of common stock may be deemed "underwriters" within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. Selling holders who are "underwriters" within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

In addition, any securities covered by this prospectus that qualify for sale pursuant to Rule 144 or Rule 144A of the Securities Act may be sold under Rule 144 or Rule 144A rather than pursuant to this prospectus. A selling holder may not sell any shares of common stock described in this prospectus and may not transfer, devise or gift these securities by other means not described in this prospectus.

To the extent required, the shares of common stock to be sold, the names of the selling holders, the respective purchase prices and public offering prices, the names of any agent, dealer or underwriter, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement of which this prospectus is a part.

In connection with the acquisition of all outstanding share capital of Bradford Particle Design plc, we agreed for the benefit of the selling security holders to register the common stock of Inhale they received under applicable federal and state securities laws under specific circumstances and at specific times. We will pay substantially all of the expenses incurred by the selling holders incident to the offering and sale of the common stock.

#### LEGAL MATTERS

The validity of the shares of common stock offered hereby is being passed upon for us by Cooley Godward LLP, Palo Alto, California.

#### EXPERTS

Ernst & Young LLP, independent auditors, have audited our financial statements included in our Annual Report on Form 10-K, as amended, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

Ernst & Young LLP, independent auditors, have also audited the financial statements of Bradford Particle Design plc, included in our Current Report on Form 8-K filed on January 11, 2001, as set forth in their report, which is incorporated by reference in the registration statement. These financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WE HAVE AUTHORIZED NO ONE TO GIVE ANY INFORMATION OR TO MAKE ANY REPRESENTATIONS THAT ARE NOT CONTAINED IN THIS PROSPECTUS. YOU SHOULD RELY ONLY ON THE INFORMATION PROVIDED IN THIS PROSPECTUS OR INCORPORATED BY REFERENCE THEREIN. YOU MUST NOT RELY ON ANY UNAUTHORIZED INFORMATION.

THIS PROSPECTUS DOES NOT OFFER TO SELL OR BUY ANY SHARES OF COMMON STOCK IN ANY JURISDICTION WHERE IT IS UNLAWFUL. YOU SHOULD NOT ASSUME THAT THE INFORMATION IN THIS PROSPECTUS IS ACCURATE AS OF ANY DATE OTHER THAN THE DATE ON THE FRONT OF THE DOCUMENT.

-----

TABLE OF CONTENTS

|  | PAGE |
|--|------|
| About our Business.....                  | 1    |
| Risk Factors.....                        | 3    |
| Where You Can Find More Information..... | 10   |
| Incorporation by Reference.....          | 10   |
| Use of Proceeds.....                     | 11   |
| Selling Security Holders.....            | 12   |
| Plan of Distribution.....                | 14   |
| Legal Matters.....                       | 15   |
| Experts.....                             | 15   |

-----

3,752,456  
SHARES  
OF COMMON STOCK