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FORM 10-K

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SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

[X] ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2000
OR
[ ] TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 (NO FEE REQUIRED)

Commission file number 1-12584

SHEFFIELD PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its Charter)

DELAWARE	13-3808303
(State of Incorporation)	(IRS Employee Identification Number)

425 SOUTH WOODSMILL ROAD	63017	(314) 579-9899
ST. LOUIS, MISSOURI	(Zip Code)	(Registrant's telephone,
(Address of principal executive offices)		including area code)

SECURITIES REGISTERED PURSUANT TO SECTION 12(b) OF THE ACT:

Title of Class	Name of each exchange on which registered
Common Stock. $.01 par value	American Stock Exchange

SECURITIES REGISTERED PURSUANT TO SECTION 12(g) OF THE ACT:

None

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.
[X]Yes [ ] No

Indicate by check mark if disclosure of delinquent filers to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. [X]

The aggregate market value at March 6, 2001 of the voting stock of the registrant held by non-affiliates (based upon the closing price of $3.70 per share of such stock on the American Stock Exchange on such date) was approximately $77,515,000. Solely for the purposes of this calculation, shares held by the registrant's directors and executive officers and beneficial owners of 10% or more of the Company's Common Stock of the registrant have been excluded. Such exclusion should not be deemed a determination or an admission by the registrant that such persons are, in fact, affiliates of the registrant.

Indicate the number of shares outstanding of each of the registrant's classes of common equity, as of the latest practicable date: At March 6, 2001, there were outstanding 28,829,276 shares of the registrant's Common Stock, $.01 par value.

DOCUMENTS INCORPORATED BY REFERENCE

Certain portions of the Company's Annual Report to Stockholders for the year ended December 31, 2000 are incorporated by reference in Items 6, 7 and 8 of this Annual Report on Form 10-K and attached as Exhibit 13 hereto.

Certain portions of the Registrant's definitive proxy statement to be filed not later than April 30, 2001 pursuant to Regulation 14A are incorporated by reference in Items 10 through 13 of Part III of this Annual Report on Form 10-K.

PART I

The following contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are intended to be covered by the safe harbors created thereby. All forward-looking statements involve risks and uncertainty. Although the Company believes that the assumptions underlying the forward-looking statements contained herein are reasonable, any of the assumptions could be inaccurate, and therefore, there can be no assurance that the forward-looking statements included in this report will prove to be accurate. The Company's actual results may differ materially from the results anticipated in the forward-looking statements. See "Business -- Certain Risk Factors that May Affect Future Results, Financial Condition and Market Price of Securities" included herein for a discussion of factors that could contribute to such material differences. In light of the significant uncertainties inherent in the forward-looking statements included herein, the inclusion of such information should not be regarded as a representation by the Company or any other person that the objectives and plans of the Company will be achieved.

ITEM 1. BUSINESS

THE COMPANY

Sheffield Pharmaceuticals, Inc. (formerly Sheffield Medical Technologies Inc.) ("Sheffield" or the "Company") was incorporated under Canadian law in October 1986. In May 1992, the Company became domesticated as a Wyoming Corporation pursuant to a "continuance" procedure under Wyoming law. In January 1995, the Company's shareholders approved the proposal to reincorporate the Company in Delaware, which was effected on June 13, 1995. The Company is a specialty pharmaceutical company focused on development and commercialization of later stage pharmaceutical opportunities utilizing proprietary pulmonary delivery technologies over a range of therapeutic areas. Through our alliances with Elan Corporation plc ("Elan"), Zambon Group SpA ("Zambon"), and Siemens AG ("Siemens"), Sheffield is currently developing nine respiratory and systemic (non-respiratory) therapies to be delivered through the Company's Metered Solution Inhaler, or MSI, and Aerosol Drug Delivery System, or ADDS. Sheffield believes these pulmonary delivery technologies will allow the Company to capitalize on the growing drug delivery market by providing both advanced respiratory treatments and patient-friendly alternatives for therapies that can currently be administered only by injection or other inconvenient means.

In 1997, the Company acquired rights to the MSI, a portable nebulizer-based pulmonary delivery system, through a worldwide exclusive license and supply arrangement with Siemens. In June 1998, Sheffield sublicensed to Zambon worldwide marketing and development rights to respiratory products to be delivered by the MSI. During the second half of 1998, the Company acquired the rights to an additional pulmonary delivery technology, the ADDS from a subsidiary of Aeroquip-Vickers, Inc. ("Aeroquip-Vickers"). The ADDS technology is a new generation propellant-based pulmonary delivery system. Additionally, during 1998, Sheffield licensed from Elan, the Ultrasonic Pulmonary Drug Absorption System ("UPDAS(TM)"), a novel disposable unit dose nebulizer system, and Elan's Absorption Enhancing Technology ("Enhancing Technology"), a therapeutic agent to increase the systemic absorption of drugs. In October 1999, the Company licensed Elan's Nanocrystal(TM) dispersion technology to be used in developing certain steroid products.

BUSINESS STRATEGY

The Company's business strategy is to seek out opportunities to acquire and develop commercially attractive pharmaceutical products, primarily in the area of pulmonary drug delivery. The Company recognizes that no single technology in the area of pulmonary drug delivery will meet the needs of patients and providers of the wide variety of compounds (both for respiratory disease and systemic disease therapy) that may benefit therapeutically and commercially from pulmonary delivery. As a result, it remains the Company's goal to acquire or in-license a portfolio of pulmonary delivery technologies to meet the broadest based market opportunity. The Company intends to selectively enter into joint ventures or other forms of strategic alliances to defray or reduce significant development and manufacturing costs associated with these opportunities that otherwise might be borne by the Company while retaining certain commercial rights.

The Company will continue to be opportunistic in the acquisition and/or

in-licensing of technologies or products that meet the Company's strategic objectives. Such opportunities include: (1) technologies or products that meet the needs of healthcare communities that are not currently served, (2) technologies or products that can effectively be developed when viewed in light of the commercial opportunity and competitive environment within the U.S. market, (3) technologies or products that will be of substantive interest to other companies with regard to co-development and co-marketing with limited incremental investment by the Company, and (4) products and technologies with the potential for marketing to a specialty group or limited physician audience. The Company plans to pay special attention to platform technologies that can be developed into multiple applications in varying therapeutic categories.

STRATEGIC ALLIANCES

The Company believes a less costly, more predictable path to commercial development of therapeutics can be achieved through the creative use of collaborations and alliances, combined with state-of-the-art technology and experienced management. The Company is applying this strategy to the development of both respiratory and systemic pharmaceutical products to be delivered through the Company's proprietary pulmonary delivery systems. Using these pulmonary delivery systems as platforms, the Company has established strategic alliances for developing its initial products with Elan, Siemens and Zambon.

In a collaboration with Zambon, the Company is developing a range of pharmaceutical products delivered by the MSI to treat respiratory diseases. Under its agreement with Zambon, MSI commercial rights for respiratory products have been sublicensed to Zambon in return for an equity investment in the Company (approximately 10%). Zambon has committed to fund the development costs for respiratory compounds delivered by the MSI, as well as make certain milestone payments and pay royalties on net sales to the Company resulting from these MSI products. Initial products for respiratory disease therapy delivered through the MSI include albuterol, ipratropium, cromolyn and inhaled steroids. The Company has maintained co-marketing rights for the U.S. The Company's ability to co-market MSI respiratory products in the U.S. requires no additional payment to Zambon by the Company. Zambon and the Company are having discussions regarding the possible modification of their agreement, including the future marketing arrangements for the MSI respiratory products in the United States.

As part of a strategic alliance with Elan, a world leader in pharmaceutical delivery technology, the Company is developing therapies for systemic diseases to be delivered to the lungs using both the ADDS and MSI. In 1998, the systemic applications of the MSI and ADDS were licensed to Systemic Pulmonary Delivery, Ltd. ("SPD"), a wholly owned subsidiary of the Company. In addition, two Elan technologies, UPDAS and the Enhancing Technology, have also been licensed to SPD. The Company has retained exclusive rights outside of the strategic alliance to respiratory disease applications utilizing the ADDS technology and the two Elan technologies. Two systemic compounds for pulmonary delivery are currently under development. For the treatment of breakthrough pain, the Company is developing morphine delivered through the MSI. Ergotamine, a therapy for the treatment of migraine headaches, is currently being developed for use in the ADDS.

In addition to the above alliance with Elan, in 1999, the Company and Elan formed a joint venture, Respiratory Steroid Delivery, Ltd. ("RSD"), a 80.1% owned subsidiary of the Company and 19.9% owned by Elan, to develop certain inhaled steroid products to treat certain respiratory diseases using Elan's

NanoCrystal(TM) dispersion technology. The inhaled steroid products to be developed include a propellant-based steroid formulation for delivery though the ADDS, a solution-based unit-dose-packaged steroid formulation for delivery using a conventional tabletop nebulizer, and a solution-based steroid formulation for delivery using the MSI system.

Outside of these alliances, the Company owns the worldwide rights to respiratory disease applications of all of its technologies, subject only to the MSI respiratory rights sublicensed to Zambon.

In addition to the above, the Company has several agreements in place for the manufacture of its delivery systems. Siemens, a multi-national engineering and electronics conglomerate, serves as the manufacturer of the MSI. Siemens also provides ongoing technical support in the design and testing of pharmaceutical products in the MSI. The interchangeable drug-containing cartridges in the MSI are being assembled and filled by Cheasapeake Biological Laboratories of Baltimore, Maryland. During 1999, the Company signed an agreement with an aerosol manufacturer, Medeva Pharmaceuticals MA, Inc., for the manufacture and supply of certain products to be delivered by the ADDS.

The Company is also currently in discussions with a number of pharmaceutical and biotechnology companies about potential collaborations for developing specific compounds (both respiratory and systemic) in the ADDS. Unlike the MSI, ADDS is a technology that lends itself to individual product applications in the respiratory market. While the ADDS technology may be applicable to a wide range of respiratory products, the Company believes that a full line of products delivered by ADDS is not necessary for commercial success. The reverse is true with the MSI, since one of the MSI's primary competitive advantages is the delivery of a range of drugs in interchangeable cartridges used with the parent nebulizer device.

PULMONARY DELIVERY MARKET ENVIRONMENT

The Company competes in the pulmonary delivery market. The principal use of pulmonary delivery has been in the treatment of respiratory diseases such as asthma, chronic obstructive pulmonary disease ("COPD") and cystic fibrosis. There is significant advantage in aerosol therapy for respiratory disease. Pulmonary administration delivers the medication directly onto the lung's epithelial surfaces. In many cases, this means that drugs can be effective in very low doses -- reducing the side effects usually associated with systemic administration. In 1998, industry sources estimate there were approximately 35.5 million asthma patients and 49.5 million COPD patients worldwide. These sources indicate that the number of newly diagnosed patients is growing at a rate in excess of 10% annually due to an increase in worldwide air pollution levels and the overall aging of the population. By the year 2005, the Company expects that there will be more than 19 million asthma patients in the United States alone.

In addition, the competitive marketplace has been significantly affected by the worldwide phase out of clorofluorocarbons ("CFCs") pursuant to the Montreal Protocol. CFCs are the propellants traditionally used in metered dose inhalers ("MDIs"), which are the most common form of pulmonary delivery. Companies in the respiratory market have initiated significant programs to

redevelop existing products using alternative propellants, dry powders or nebulizers.

There is considerable interest in applying pulmonary delivery technology to systemic therapies that would benefit from the relatively easy administration to the circulatory system through the lungs. Work on pulmonary delivery of insulin by other pulmonary delivery companies has received significant public notice. There is a range of therapies that could provide a significant market opportunity if available in a pulmonarily delivered form.

Today, three types of devices are widely used in pulmonary drug administration: metered dose inhalers, dry powder inhalers, and nebulizers.

Metered Dose Inhalers. Currently, MDIs are the most commonly used pulmonary delivery system. It is estimated that in the United States 80% of pulmonary drug delivery is via MDI, with the majority of this use coming from adults with asthma and COPD.

The main components of an MDI include a canister containing the drug mixed with propellant and surfactant, a mouthpiece that acts as the delivery conduit and the actuator seat for the release of the drug. The initial velocity of particles as they leave an inhaler is very high -- approximately 2-7 meters per second -- resulting in wasted drug if the patient is not able to coordinate his/her breath with the delivery of aerosol into the mouth. A number of studies have demonstrated that as many as 60% of patients cannot accurately time their inspiration with the actuation of their inhaler which results in under medication and lack of compliance. Typically, less than 20% of delivered drug actually reaches the lungs.

The primary advantages of an MDI include its small size, portability, fast usage time, and its availability for use with most respiratory drugs. Disadvantages of an MDI include patient coordination issues and efficient dose delivery. Additionally, because the use of CFCs traditionally used in MDIs are being phased out by international agreement (Montreal Protocol), alternative propellants and formulations are being developed. Over time, all current MDI users will be required to move to a non-CFC MDI or other alternative delivery systems. The majority of U.S. patients favor aerosol MDIs although a sizable percentage may not coordinate them properly.

Dry Powder Inhalers. Dry powder inhalers ("DPIs") were introduced in the 1960s as single-dose inhalers. In these devices, the drug is loaded as a unit dose that is mechanically released as a powder for inhalation prior to each use. To date, these relatively cumbersome systems have been the primary form of DPI available in the United States, and account for approximately 1% of the total aerosol delivery market.

The inconvenience of the single dose DPI has been overcome outside of the U.S. with the development and introduction of multi-dose DPIs that can deliver up to 200 doses of medication. However, like the single dose systems, they are inspiratory flow rate dependent; that is, the amount of drug delivered to the lung depends on the patient's ability

to inhale.

Two of the most significant advantages of DPIs include (1) no hand-breath coordination is required as with MDIs; and (2) they contain no CFCs. However, most require a high inspiratory flow rate, which can be problematic in younger patients or patients with compromised lung function. In addition, they often present difficulties for those with manual disabilities (e.g., arthritis) or limited vision and, depending upon the powder load delivered, they may induce acute bronchospasm in sensitive individuals. Additionally, multi-dose powder inhalers are subject to moisture sensitivity either from the environment or patient breath and have had difficulty meeting U.S. regulatory standards for dose-to-dose variation.

Nebulizers. The third widely-used aerosol delivery system is the nebulizer. Jet nebulizers, which are the most commonly used nebulizer, work on a stream of compressed air or oxygen that is forced through a narrow tube lying just above the surface of the liquid to be nebulized. It takes approximately 10 to 15 minutes to nebulize this amount of liquid. Studies suggest keeping the duration of nebulization below 10 minutes, as longer durations are associated with poor compliance. During nebulization only about 10% of the drug is delivered to the lungs; about 80% gets trapped in the reservoir, tubing and mask; the rest is exhaled.

Nebulizers can be used for a wide range of patients, but are especially useful for those older and younger patients who cannot manage other inhaler devices. Nebulizers also play a key role in emergency room and intensive care treatment for patients with acute bronchospasm. Another feature exclusive to nebulizers is that a mixture of drugs can be administered in one sitting. However, currently approved nebulizers are bulky table-top units that are time consuming, have a high initial cost (often in excess of the amount reimbursable by managed care) and can be noisy during operation.

METERED SOLUTION INHALER

The MSI pulmonary drug delivery system has been developed to provide the therapeutic benefit of nebulization with the convenience of pressurized MDIs in one system. The MSI was developed to meet specific needs within the respiratory market, particularly for pediatric and geriatric patients suffering from asthma and COPD.

Description of the MSI

The MSI is comprised of two main components: (1) a reusable, pocket-size inhaler unit developed and manufactured for the Company by Siemens; and (2) drug cartridges containing multiple doses of drug formulation assembled and filled by Chesapeake Biological Laboratories. The cartridges are an integral part of the total system. The cartridge plus each drug formulation will be the subject of a separate drug device combination New Drug Application ("NDA").

The basic technology of the system involves the rapid nebulization of therapeutic agents using ultrasonic waves. This produces a concentrated cloud of medication delivered through the mouthpiece over a two to three second period for inhalation. The key components of the technology are housed in the inhaler

unit. They are the rechargeable battery-operated motor, ultrasonic horn and drug cartridge. The pocketsize MSI allows for administration of a range of drugs in a single, simple-to-use, environmentally friendly delivery system. Each cartridge contains, depending on formulation, approximately a one to two month supply of the drug.

To use the MSI system, a patient simply selects the appropriate color-coded drug cartridge and places it into the chamber of the inhaler unit. Pressing the "on" button activates a small electrical motor that transports a precise dose of drug from the cartridge chamber to the ultrasonic horn -- transforming the solution into an aerosolized cloud. The patient's inspiratory breath carries this cloud of medication directly to the lungs where it is needed. The dose delivered by the MSI is very accurate and consistent because: (1) the MSI is designed to be inspiratory flow rate independent; that is, delivery of the drug does not depend upon the patient's ability to inhale forcefully, and (2) the MSI does not require a high level of coordination between inspiration and actuation of the device. The patient's natural breath carries the medication directly to the lungs, minimizing the amount of drug deposited in the mouth and throat.

MSI Advantages

The Company believes that the MSI provides significant advantages over other drug delivery systems. It is particularly suited for younger and older asthma patients, as well as for older COPD patients who have difficulty using MDIs and currently have to depend on larger, more time-consuming tabletop nebulizers for delivery of their medications. These potential advantages include:

- Accuracy. The superior engineering and patient-friendly design of the MSI is intended to provide minimal dose-to-dose variability. Patients can therefore expect to receive the right therapeutic dose consistently. Testing of the MSI system has shown that dose-to-dose variability with the MSI is significantly better than the current FDA requirement.

- Enhanced Patient Compliance. The pocketsize, portable MSI unit is designed to combine the therapeutic benefits of nebulization with the convenience of pressurized metered dose inhalers. The drug dose is precisely measured and delivered in seconds, as compared to 10 to 15 minutes or more for the typical nebulizer. The device is easy to operate, requiring minimal coordination between actuation and inhalation for proper drug delivery. These benefits are expected to improve patient compliance with the proper administration of their respiratory medication. Another expected factor in enhanced patient compliance is the broad range of drugs that can be accommodated by the MSI, allowing patients on multiple medications to rely on one simple delivery system.

- Inspiratory Flow Rate Independence. Unlike most of the DPIs currently available (or in development), the MSI is designed to achieve a consistent and significant level of drug deposition over a broad range of inspiratory flow rates. This is especially important in younger

patients or patients with compromised lung function (e.g., during an asthma attack) who have a difficult time breathing normally.

Versatility. Many asthma and COPD patients are taking multiple inhalation medications. The MSI accommodates drug cartridges to allow for the administration of a broad range of frequently used respiratory drugs in a single, simple-to-use delivery system. The system includes an early warning mechanism that signals when the batteries need recharging or when the dosator is not functioning properly and a dose counter indicating when a new inhaler unit is required. These user-friendly features result in a simplified dosing procedure for both patients and their caregivers.

Pulmonary Targeting. The particle size of the inhaled medication affects the effectiveness of drug delivery to the lung. Generally, a drug is "respirable" if the particle size is between two and five microns. Larger particles tend to deposit in the inhaler or in the patient's mouth and throat. Smaller particles tend to be exhaled. Within the respirable range, the MSI is designed to deliver particles specifically targeted for certain portions of the lungs; for example, the central lung for local treatment or the deep lung for enhanced absorption into the blood stream for systemic therapies.

Environmentally Friendly. CFCs, the most commonly used propellant for MDI aerosols, are believed to adversely affect the Earth's ozone layer. They are subject to worldwide regulations aimed at eliminating their production and use within the decade under the Montreal Protocol. The MSI does not use CFCs or any other type of ozone depleting propellant.

Economical. The Company believes that the MSI offers significant value to the patient because it is designed to allow a single device to be used with a complete family of respiratory medications available in cost-effective interchangeable cartridges. The inhaler unit itself is expected to have a life of two to three years. The initial cost of the inhaler unit is expected to be within the cost range that managed care providers will reimburse patients. The Company anticipates the combined cost to the patient of the device plus the drug filled cartridges will be comparable to the average cost per dose of the standard metered dose inhaler.

MSI Product Pipeline in Development

The Company is implementing a broad development strategy for the MSI. The Company and Zambon are developing a range of widely used respiratory drugs for delivery in the MSI. Potential candidates for respiratory disease therapy include albuterol, ipratropium, cromolyn, inhaled bronchial steroids and combination products, each of which is described below. Most patients who experience respiratory disease commonly use multiple medications to treat their conditions.

Among the drugs being developed for respiratory applications in the MSI system

are:

ALBUTEROL. Albuterol is a beta agonist used as rescue therapy for patients with asthma and COPD. It is the largest selling respiratory compound with U.S. sales of over $500 million in all dosage forms. It is available in a metered dose inhaler and nebulizer solution as well as solid and liquid dosage forms.

Status: Zambon initiated a Phase II clinical trial in December 1999 which compared the MSI to a conventional albuterol-MDI. Findings from Phase II studies indicated that MSI-albuterol and MDI-albuterol were comparable in improving lung function in the 24 adult patients. An end of Phase II meeting has been scheduled with the Food and Drug Administration ("FDA").

IPRATROPIUM. Ipratropium is a bronchodilator used primarily to treat COPD patients. It is useful because of its anticholinergic properties, which reduce pulmonary congestion. It is available in a metered dose inhaler, nebulizer solution and a combination product with albuterol.

Status: Zambon initiated a Phase I/II clinical trial in Europe in January 2000 assessing the safety and efficacy compared to a commercially available ipratropium product delivered by a MDI and placebo in patients with COPD. The results of the study indicated that both MSI-ipratropium and MDI-ipratropium improved lung function in the COPD patients. An Investigational New Drug Application ("IND") was filed with the FDA- in May 2000.

CROMOLYN. Cromolyn is a non-steroidal, anti-inflammatory drug used to reduce the underlying bronchial inflammation associated with asthma. It is extremely safe and it is most commonly used to treat pediatric patients. It is available in a MDI and nebulizer solution.

Status: An IND was filed with the FDA in July 2000.

INHALED BRONCHIAL STEROIDS. Inhaled bronchial steroids are anti-inflammatory agents. They address the underlying inflammation in the lungs of asthma and COPD patients. They are available in a metered dose inhaler. Steroids are the fastest growing category in the respiratory market, growing at 20% per year.

Status: Formulation work is currently underway. An IND is being prepared for filing with the FDA.

OTHER RESPIRATORY THERAPIES. In addition to the drugs listed above, the Company and Zambon are assessing the market potential for certain other respiratory therapies. These therapies may include a combination of an anti-inflammatory and beta agonist, and an anticholinergic and beta agonist, as well as antibiotics, cystic fibrosis treatments and a range of early stage biotech compounds that target respiratory disease.

SYSTEMIC APPLICATIONS: Through its development alliance with Elan, the Company is currently evaluating certain drugs for systemic treatment by pulmonary delivery through the MSI. The first of these drugs, morphine, is for

the treatment of severe pain. The pain management market includes patients with cancer, post-operative, migraine headache and chronic persistent pain. Narcotic analgesics for treatment of these severe forms of pain are estimated to exceed $1.0 billion in worldwide sales in the year 2000. The Company has identified a market opportunity for a rapid-acting, non-invasive treatment for breakthrough pain.

Status: In July 1999, the Company completed a gamma scintigraphy/pharmacokinetic trial comparing morphine delivered via the MSI to subcutaneous injection. The MSI demonstrated good pulmonary deposition and very rapid absorption, more rapid peak blood levels vs. subcutaneous injection and low oral and throat deposition. The Company is currently seeking to attract a partner for the continued development and commercialization of this product.

AEROSOL DRUG DELIVERY SYSTEM

The ADDS, a new generation MDI, was developed to correct major deficiencies associated with existing MDI technology. MDIs have provided convenient, safe, self-administered treatment for over 30 years and decrease the cost of therapy because they can be used by the patient at home with minimal medical supervision. However, proper use of current MDIs requires training and precise execution of the delivery technique. For these reasons, many patients do not use their MDIs in the prescribed manner to coordinate actuation and inhalation. Incorrect technique has been shown to result in little or no benefits from MDI use in half of all adult patients and in a greater proportion of children. Moreover, because of these coordination issues, most children under age five cannot use a standard MDI.

Even with correct technique, current MDIs typically deliver less than 20% of the drug to the lungs of the patient. The remainder of the drug is wasted upon deposition on the back of the mouth, or by completely missing the airway. This results from: (1) the high linear velocity (two to seven meters/second) of the aerosol jet as it discharges; (2) incomplete evaporation of the propellant leading to large size droplets that deposit in the mouth and larynx rather than reaching the lung; and (3) inadequate mixing resulting in a non-uniform distribution of drug particles in the inspiratory flow stream. Drug deposited in the mouth and throat can be swallowed and absorbed systemically or, in the case of inhaled steroids, may create a local concentration of the drug that causes immunosuppression response and the development of fungal infections. In addition, swallowing beta agonist bronchodilators may result in adverse effects on heart rate, blood pressure, glucose and potassium.

From a therapeutic view, the most serious problem with MDIs is inconsistency of delivery. With existing MDIs the actual dose can vary from 0% to 300% of the intended dose. Patients may not receive sufficient drug to achieve a therapeutic effect, or they may overdose with undesirable side effects. These conditions can lead to the need for emergency treatment.

A major advantage for the ADDS technology is that it uses the same aerosol canisters and valves as are currently used in existing MDIs. As a result, existing aerosol facilities will be able to produce canisters with formulations optimized for use in ADDS. The only additional step required is to place the aerosol canister in the "device" prior to final packaging. This

results in a cost effective product and provides numerous benefits to patients. The device along with the canister are disposable when the canister is empty.

The ADDS technology features two improvements over existing MDIs and dry powder inhalers. Fluid dynamics modeling, in-vitro and human trials indicate that up to 50% of drug emitted by the ADDS reaches the lungs with oral deposition reduced to approximately 10%. Because of this increase in efficiency, ADDS should require less drug per actuation than existing devices to achieve the same therapeutic effect. This may result in more unit doses per drug canister than a conventional MDI, with less potential for adverse reactions.

ADDS also features a unique proprietary triggering mechanism that actuates at the correct time during inhalation. It is designed to automatically adjust to the patient's breathing pattern to accommodate differences in age and disease state. This synchronous trigger is designed to reduce patient coordination problems and enhance patient compliance.

Description of the ADDS

The ADDS technology utilizes a standard aerosol MDI canister, encased in a compact device that provides an aerosol flow-control chamber and a synchronized triggering mechanism. Manipulation of the discharged drug-containing aerosol cloud is key to optimization of the efficiency and consistency for MDIs.

The ADDS design uses fluid dynamics to: (1) reduce the velocity of the drug relative to the inspiratory breath velocity (less than one meter/second); (2) increase residence time of the aerosol droplets before exiting the device to allow near complete evaporation of the propellant; (3) increase droplet dispersion and mixing, thus increasing evaporation and improving vapor fraction at every point along the flow path; (4) reduce the diameter of the drug particles at the exit plane of the device; (5) decrease inertia of droplets to reduce impaction; and (6) improve timing of dose discharge with inspiratory breath for increased drug deposition in lungs.

The unique features of ADDS are:

Aerosol Flow-Control Chamber. The aerosol flow-control chamber allows the patient to inhale through the device at a normal breathing rate, instead of a forced breath. The inspiratory breath establishes flow fields within the device that mix and uniformly disperse the drug in the breath. In the mouthpiece, nearly all the propellant is evaporated leaving only drug particles to be inspired, allowing a significant increase in the amount of drug delivered to the lungs. Only small amounts of drug deposit in the mouth and throat.

Synchronizing Trigger Mechanism. A triggering and timing mechanism that is synchronized with the patient's inspiratory breath controls the discharge of the metering valve. ADDS can accommodate different inspiratory flowrates, so any patient can activate the triggering device. Similarly, the timing mechanism will automatically adjust to the flow generated by the patient, delaying or hastening discharge in proportion to the total volume passing through the flow control chamber. This feature accommodates differences in inspiratory flow

characteristic of pulmonary disease states in children, adults and the infirm.

ADDS Advantages

The Company believes that the ADDS technology possesses many potential competitive advantages over other inhalation systems in both local respiratory and systemic applications. It is applicable to all age categories, eliminating the most troublesome problems of aerosol metered dose delivery. Increased efficiency allows for potential application to proteins and peptides formerly not considered as candidates for aerosol delivery.

The performance characteristics of the ADDS are expected to translate into multiple benefits, including:

Improved Drug Delivery Efficiency. A higher percentage of the drug emitted by the ADDS is delivered to the lungs than current inhalation systems while approximately 10% is lost through deposition in the mouth and throat. The improved delivery efficiency enhances efficacy, reduces side effects and provides greater consistency of dose administration.

Greater Patient Compliance. The ADDS reduces technique dependence for simple, consistent dose-to-dose delivery, resulting in improved compliance with prescribed therapy.

Broader Patient Base. The ADDS can be prescribed for a broader patient base since it is designed to be self-administered by children and the elderly as well as adult patients.

Pharmacoeconomic Benefit. The ADDS has increased delivery efficiency with less waste, so patients can receive more unit doses per standard canister. This allows for a lower drug cost per day in addition to reducing prescription and payor costs because fewer pharmacy visits are required.

ADDS Product Pipeline in Development

ADDS SYSTEMIC THERAPIES. The development of systemic drugs using ADDS is being conducted as part of the Company's alliance with Elan. The first product to be developed is targeted to address migraine headaches. The Company is utilizing ergotamine tartrate as a proof-of-principle product. Ergotamine, an alpha adrenergic blocking agent, is a therapy to stop or prevent vascular headaches such as migraines. Migraine headaches affect 16-18 million Americans. Worldwide annual sales for the migraine therapy market are in excess of $2.3 billion with many patients unable to get satisfactory relief from currently available therapies. In fact, it is estimated that absenteeism and medical expenses resulting from migraine total $50 billion annually. Current oral drug therapies for the treatment of migraine headaches have slow onset of action, resulting in a medical need that may be better satisfied through pulmonary delivery.

Status: In December 1999, the Company completed a gamma scintigraphy/pharmacokinetic trial comparing the ADDS to a conventional MDI. The trial showed successful delivery of the drug to all regions of lung with significantly reduced mouth and throat deposition, and rapid drug absorption. The Company is currently seeking to attract a partner for the continued

development and commercialization of this product.

ADDS RESPIRATORY THERAPIES. The ADDS has broad applicability across respiratory disease therapies since it utilizes basic MDI delivery methods that are the most popular forms of respiratory delivery. The ADDS technology's ability to significantly minimize oral deposition makes it especially applicable to steroids and steroid combinations with which fungal overgrowth side effects are common. In addition, U.S. patients and physicians have indicated that they prefer metered dose aerosol delivery. The ADDS technology is positioned to take advantage of this built-in market preference for MDIs with its potential for superior performance, reduced adverse reactions and cost-effectiveness. Inhaled steroids are the fastest growing segment of the respiratory market and the largest in Europe. The features of the ADDS directly minimize the aspects of inhaled steroids that remain a concern to patients and physicians. The market for inhaled steroids on a worldwide basis is approximately $2.0 billion.

Status: In September 2000, the Company completed a pilot study using the ADDS to deliver an undisclosed, patented respiratory drug used to treat asthma. The study measured the distribution of this respiratory drug delivered by ADDS compared to the distribution of this same drug delivered through a commercially available MDI in 12 healthy volunteers. Results of this study demonstrated that ADDS significantly increased drug deposition in all regions of the lung. ADDS delivered approximately 200% more drug to the lungs, deposited approximately 75% less drug in the mouth, and increased dosing consistency by approximately 55% compared to the currently marketed form of this same drug. An IND is being prepared for filing with the FDA on this respiratory drug.

As with MSI, there remains opportunities for developing ADDS for a range of therapies either directly by the Company or in collaboration with strategic partners. Unlike the MSI, it is potentially advantageous for the Company to partner on a product-by-product basis, concentrating on prime partners to launch the system commercially and to aid in subsequent development with products developed specifically for exclusive commercialization by the Company.

INHALED STEROID PRODUCTS

In October 1999, the Company and Elan formed a separate joint venture to develop three inhaled steroid products to treat certain respiratory diseases that will utilize Elan's Nanocrystal dispersion technology and Sheffield's pulmonary delivery systems. Because of the difficulties in formulating steroids for delivery through a solution-based inhalation system, only one steroid product is currently available in the United States for delivery through a nebulizer. The estimated worldwide market for inhaled steroids is $2 billion annually and growing at 20% per year. The three products being formulated using Elan's Nanocrystal technology are 1) a propellant-based steroid formulation for inhalation in the ADDS; 2) a unit-dose packaged steroid formulation for inhalation delivery in a standard commercial tabletop device; and 3) a steroid formulation for inhalation delivery using the MSI. Formulation work is currently underway in all three of these inhaled steroid products.

ULTRASONIC PULMONARY DRUG ABSORPTION SYSTEM

The UPDAS(TM) is a novel ultrasonic pulmonary delivery system designed by Elan as a disposable unit dose nebulizer system. UPDAS was designed primarily for the delivery of proteins, peptides and other large molecules to the lungs for absorption into the bloodstream. Elan's preliminary research with UPDAS demonstrated unique atomization that may prevent denaturing of bioactive molecules and particle size distribution that meets the targets for local and systemic delivery.

ABSORPTION ENHANCING TECHNOLOGY

As part of the same transaction in which the Company acquired UPDAS, the Company also acquired a worldwide exclusive license to Elan's Absorption Enhancing Technology. While not a delivery system itself, the Enhancing Technology is a therapeutic agent identified by Elan to increase the systemic absorption of drugs delivered to the lungs. The Enhancing Technology will be utilized in conjunction with the Company's other pulmonary delivery systems.

EARLY STAGE RESEARCH PROJECTS

As part of the Company's focus on later stage pharmaceutical opportunities, the Company is seeking to out-license its portfolio of early stage medical research projects to companies that are committed to early stage biotechnology opportunities. The Company has determined that its early stage technologies do not fit the Company's pulmonary drug delivery strategy. Consequently, the Company plans to out-license these technologies while maintaining an interest in the technologies' promise without incurring the development costs associated with early stage research and development.

Because the Company is no longer funding these projects, it is at risk of losing its rights to certain of these technologies. There can be no assurance that the Company will be able to sell or license its rights to any of its remaining early stage research projects or realize any milestone payments or other revenue from those early stage research projects that have been previously divested.

In November 1997, the Company entered into a license arrangement for some of its early stage technologies with Lorus Therapeutics, Inc. (formerly Imutec Pharma Inc.). The arrangement licenses rights to a series of compounds for the treatment of cancer, Kaposi's sarcoma and actinic keratosis to a newly formed company, NuChem Pharmaceuticals, Inc. ("NuChem") for which Lorus Therapeutics will provide funding and management of the development program. The Company holds a 20% equity interest in NuChem.

Work on the lead compounds by NuChem has progressed in the pre-clinical phase. In 1999, NuChem announced that the U.S. National Cancer Institute has agreed to undertake additional in vitro screening after initial evaluation of the compounds. In 2000, NuChem chose NC 381 as its lead anti-cancer drug for further studies in preparation for clinical trials. Preclinical toxicology studies are currently underway.

GOVERNMENT REGULATION

The Company's research and development activities and, ultimately, any

production and marketing of its licensed products, are subject to comprehensive regulation by numerous governmental authorities in the United States and other countries. Among the applicable regulations in the United States, pharmaceutical products are subject to the Federal Food, Drug & Cosmetic Act, the Public Health Services Act, other federal statutes and regulations, and certain state and local regulations. These regulations and statutes govern the development, testing, formulation, manufacture, labeling, storage, record keeping, quality control, advertising, promotion, sale, distribution and approval of such pharmaceutical products. Failure to comply with applicable requirements can result in fines, recall or seizure of products, total or partial suspension of production, refusal by the government to approve marketing of the product and criminal prosecution.

A new drug may not be legally marketed for commercial use in the United States without FDA approval. In addition, upon approval, a drug may only be marketed for the indications, in the formulations and at the dosage levels approved by the FDA. The FDA also has the authority to withdraw approval of drugs in accordance with applicable laws and regulations. Analogous foreign regulators impose similar approval requirements relating to commercial marketing of a drug in their respective countries and may impose similar restrictions and limitations after approval.

In order to obtain FDA approval of a new product, the Company and its strategic partners must submit proof of safety, efficacy, purity and stability, and the Company must demonstrate validation of its manufacturing process. The testing and application process is expensive and time consuming, often taking several years to complete. There is no assurance that the FDA will act favorably or quickly in reviewing such applications. With respect to patented products, processes or technologies, delays imposed or caused by the governmental approval process may materially reduce the period during which the Company will have the exclusive right to exploit them. Such delays could also affect the commercial advantages derived from proprietary processes. As part of the approval process, the FDA reviews the Drug Master File (the "DMF") for a description of product chemistry and characteristics, detailed operational procedures for product production, quality control, process and methods validation, and quality assurance. As process development continues to mature, updates and modifications of the DMF are submitted.

The FDA approval process for a pharmaceutical product includes review of (i) chemistry and formulations, (ii) preclinical laboratory and animal studies, (iii) initial IND clinical studies to define safety and dose parameters, (iv) well-controlled IND clinical trials to demonstrate product efficacy and safety, followed by submission and FDA approval of a New Drug Application (the "NDA"). Preclinical studies involve laboratory evaluation of the product and animal studies to assess activity and safety of the product. Products must be formulated in accordance with United States Good Manufacturing Procedures ("GMP") requirements and preclinical tests must be conducted by laboratories that comply with FDA regulations governing the testing of drugs in animals. The results of the preclinical tests are submitted to the FDA as part of the IND application and are reviewed by the FDA prior to granting the sponsor permission to conduct clinical studies in human subjects. Unless the FDA objects to an IND application, the application will become effective 30 days following its receipt by the FDA. There can be no certainty that submission of an IND will result in FDA authorization to commence clinical studies.

Human clinical trials are typically conducted in three sequential phases with some amount of overlap allowed. Phase I trials normally consist of testing the product in a small number of normal volunteers for establishing safety and pharmacokinetics using single and multiple dosing regiments. In Phase II, the continued safety and initial efficacy of the product are evaluated in a limited patient population, and appropriate dosage amounts and treatment intervals are determined. Phase III trials typically involve more definitive testing of the appropriate dose for safety and clinical efficacy in an expanded patient population at multiple clinical testing centers. A clinical plan, or "protocol," accompanied by the approval of the institution participating in the trials, must be submitted to the FDA prior to commencement of each clinical trial phase. Each clinical study must be conducted under the auspices of an Institutional Review Board (the "IRB") at the institution performing the clinical study. The IRB is charged with protecting the safety of patients in trials and may require changes in a protocol, and there can be no assurance that an IRB will permit any given study to be initiated or completed. In addition, the FDA may order the temporary or permanent discontinuation of clinical trials at any time. The Company must rely on independent investigators and institutions to conduct these clinical studies.

All the results of the preclinical and clinical studies on a pharmaceutical product are submitted to the FDA in the form of an NDA for approval to commence commercial distribution. The information contained in the DMF is also incorporated into the NDA. Submission of an NDA does not assure FDA approval for marketing. The application review process often requires 12 months to complete. However, the process may take substantially longer if the FDA has questions or concerns about a product or studies regarding the product. In general, the FDA requires two adequate and controlled clinical studies demonstrating efficacy with sufficient levels of statistical assurance. However, additional support may be required. The FDA also may request additional information relating to safety or efficacy, such as long-term toxicity studies. In responding to an NDA, the FDA may grant marketing approval, require additional testing and/or information, or deny the application. Accordingly, there can be no assurance about any specific time frame for approval, if any, of products by the FDA or foreign regulatory agencies. Continued compliance with all FDA requirements and conditions relative to an approved application, including product specifications, manufacturing process, labeling and promotional material, and record keeping and reporting requirements, is necessary throughout the life of the product. In addition, failure to comply with FDA requirements, the occurrence of unanticipated adverse effects during commercial marketing or the result of future studies, could lead to the need for product recall or other FDA-initiated actions that could delay further marketing until the products or processes are brought into compliance.

The facilities of each pharmaceutical manufacturer must be registered with and approved by the FDA as compliant with GMP. Continued registration requires compliance with standards for GMP. In complying with GMP, manufacturers must continue to expend time, money and effort in production, record keeping and quality control to ensure technical compliance. In addition, manufacturers must comply with the United States Department of Health and Human Services and similar state and local regulatory authorities if they handle controlled substances, and they must be registered with the United States Drug Enforcement Administration and similar state and local regulatory authorities if they generate toxic or dangerous waste streams. Other regulatory agencies such as the Occupational Safety and Health Administration also monitor a manufacturing

facility for compliance. Each of these organizations conducts periodic establishment inspections to confirm continued compliance with its regulations. Failure to comply with any of these regulations could mean fines, interruption of production and even criminal prosecution.

For foreign markets, a pharmaceutical company is subject to regulatory requirements, review procedures and product approvals which, generally, may be as extensive, if not more extensive, as those in the United States. Although the technical descriptions of the clinical trials are different, the trials themselves are often substantially the same as those in the United States. Approval of a product by regulatory authorities of foreign countries must be obtained prior to commencing commercial product marketing in those countries, regardless of whether FDA approval has been obtained. The time and cost required to obtain market approvals in foreign countries may be longer or shorter than required for FDA approval and may be subject to delay. There can be no assurance that regulatory authorities of foreign countries will grant approval. The Company has no experience in manufacturing or marketing in foreign countries nor in matters such as currency regulations, import-export controls or other trade laws.

PATENTS AND TRADEMARKS

MSI System Patents and Trademark

Under its agreement with Siemens for the technology underlying the MSI system, the Company is responsible for jointly financing and prosecuting the U.S. patent applications for the benefit of the owners and licensors of this technology. To date, three U.S. patents have issued, and two U.S. and European applications each are pending. The issued U.S. patents provide protection through 2017 for the MSI device, the dosator cartridges and their combinations.

Aerosol Drug Delivery System Patents

As of the December 31, 2000, three U.S. patents have issued and two U.S. and four foreign applications are pending. The issued U.S. patents cover the ADDS flow control and triggering mechanism through 2018.

Early Stage Research Technology Patents

Under its license agreements for its early stage research projects, the Company has been responsible for financing and prosecuting patent applications for the benefit of the owners and licensors of these technologies. While the Company holds, or has held, several U.S. and foreign patents and patent applications for these early stage technologies, the Company expects to assign these patents and applications to future acquirors, if any, of these technologies. Because the Company does not intend to continue to pay for future patent fees on these early stage technologies, in the event that no acquirors are found for these technologies, the Company expects that it will allow some or all of these patents and patent applications to lapse or the rights may be returned to the licensors.

COMPETITION

The Company competes with approximately 25 other companies involved in

developing and selling respiratory products for the U.S. market. Most of these companies possess financial and marketing resources and developmental capabilities substantially greater than the Company. Some of the products in development by other companies may be demonstrated to be superior to the Company's current or future products. Furthermore, the pharmaceutical industry is characterized by rapid technological change and competitors may complete development and reach the marketplace prior to the Company. The Company believes that competition in the respiratory category will be based upon several factors, including product efficacy, safety, reliability, availability, and price, among others.

SUBSIDIARIES

On January 10, 1996, Ion Pharmaceuticals, Inc. ("Ion"), was formed as a wholly owned subsidiary of the Company. At that time, Ion acquired the Company's rights to certain early stage biomedical technologies.

On April 17, 1997, CP Pharmaceuticals, Inc. ("CP") was formed for the purpose of acquiring Camelot Pharmacal, LLC ("Camelot"), a privately held pharmaceutical development company. The Company acquired Camelot on April 25, 1997.

As part of its strategic alliance with Elan, on June 30, 1998, the Company formed SPD as a wholly owned subsidiary. At that time, SPD acquired the Company's rights to the systemic applications of the MSI and the ADDS. In addition, SPD acquired Elan's rights to the UPDAS and the Enhancing Technology. SPD is responsible for the development of systemic applications in both the MSI and ADDS.

In addition to the above alliance with Elan, on October 18, 1999, the Company and Elan formed a new joint venture, RSD, to develop certain respiratory steroid products. The Company and Elan made equity investments in RSD representing an initial 80.1% and 19.9%, respectively, ownership in the joint venture. The joint venture is responsible for the development of the inhaled steroid products.

EMPLOYEES

As of March 6, 2001, the Company employed 17 persons, five of whom are executive officers.

CERTAIN RISK FACTORS THAT MAY AFFECT FUTURE RESULTS, FINANCIAL CONDITION AND MARKET PRICE OF SECURITIES

The following are some of the factors that could affect the Company's future results. They should be considered in connection with evaluating forward-looking statements contained in this report and otherwise made by the Company or on the Company's behalf, because these factors could cause actual results and conditions to differ materially from those projected in forward-looking statements.

We have experienced significant operating losses throughout our history and expect these losses to continue for the foreseeable future.

Our operations to date have consumed substantial amounts of cash and we have generated to date only limited revenues from contract research and licensing activities. We have incurred approximately $80.8 million of operating losses since our inception, including $6.1 million during the year ended December 31, 2000. Our operating losses and negative cash flow from operations are expected to continue in the foreseeable future.

We will need additional financing, which if not available, could prevent us from funding or expanding our operations.

Cash available for funding our operations as of December 31, 2000 was $3.0 million. As of such date, we had trade payables and accrued liabilities of $1.2 million and current research obligations of $.2 million. In addition, committed and/or anticipated funding of research and development after December 31, 2000 is estimated at approximately $3.1 million, of which $3.0 million has been committed to be funded by Elan through the issuance of our Series E cumulative convertible preferred stock. Since December 31, 2000 we have received $1.0 million as an interest-free advance against future milestone payments, and anticipate that we have sufficient cash to meet our cash requirements through December 31, 2001, assuming we do not incur unexpected costs.

We need to raise substantial additional capital to fund our operations. The development of our technologies and proposed products will require a commitment of substantial funds to conduct costly and time-consuming research, preclinical and clinical testing, and to bring any such products to market. Our future capital requirements will depend on many factors, including continued progress in developing and out-licensing our pulmonary delivery technologies, our ability to establish and maintain collaborative arrangements with others and to comply with the terms thereof, receipt of payments due from partners under research and development agreements, progress with preclinical and clinical trials, the time and costs involved in obtaining regulatory approvals, the cost involved in preparing, filing, prosecuting, maintaining and enforcing patent claims, the need to acquire licenses to new technology and the status of competitive products.

We intend to seek such additional funding through collaborative or partnering arrangements, the extension of existing arrangements, or through public or private equity or debt financings. Additional financing may not be available on acceptable terms or at all. If we raise additional funds by issuing equity securities, stockholders may be further diluted and such equity securities might have rights, preferences and privileges senior to those of our current stockholders. If adequate funds are not available, we may be required to delay, reduce the scope of, or eliminate one or more of our research or development programs or obtain funds through arrangements with collaborative partners or others that may require us to relinquish rights to certain of our technologies, product candidates or products that we would otherwise seek to develop or commercialize. If adequate funds are not available from operations or additional sources of funding, our business will suffer a material adverse effect.

~~Our products are still in development and we may be unable to bring our products to market.~~

~~We have not yet begun to generate revenues from the sale of products. Our products will require significant additional development, clinical testing and investment prior to their commercialization. We do not expect regulatory approval for commercial sales of any of our products in the immediate future. Potential products that appear to be promising at early stages of development may not reach the market for a number of reasons. Such reasons include the possibility that products will not be proven to be safe and efficacious in clinical trials, that they will not be able to meet applicable regulatory standards or obtain required regulatory approvals, that they cannot be produced in commercial quantities at reasonable costs or that they fail to be successfully commercialized or fail to achieve market acceptance.~~

~~If our products are not accepted by the medical community, our business will suffer.~~

~~Commercial sales of our products will substantially depend upon the products' efficacy and on their acceptance by the medical community. Widespread acceptance of our products will require educating the medical community as to the benefits and reliability of the products. Our products may not be accepted and, even if accepted, we are unable to estimate the length of time it would take to gain such acceptance.~~

~~We will be required to make royalty payments on products we may develop, reducing the amount of revenues with which we could fund ongoing operations.~~

~~The owners and licensors of the technology rights acquired by us are entitled to receive a certain percentage of all revenues received by us from commercialization, if any, of products in respect of which we hold licenses. Accordingly, in addition to our substantial investment in product development, we will be required to make substantial payments to others in connection with revenues derived from commercialization of products, if any, developed under licenses we hold. Consequently, we will not receive the full amount of any revenues that may be derived from commercialization of products to fund ongoing operations.~~

~~Our dependence on third parties for rights to technology and the development of our products could harm our business.~~

~~Under the terms of existing license agreements, we are obligated to make certain payments to our licensors. In the event that we default on the payment of an installment under the terms of an existing licensing agreement, our rights thereunder could be forfeited. As a consequence, we could lose all rights under a license agreement to the related licensed technology, notwithstanding the total investment made through the date of the default. Unforeseen obligations or contingencies may deplete our financial resources and, accordingly, sufficient resources may not be available to fulfill our commitments. If we were to lose our rights to technology, we may be unable to replace the licensed technology or be unable to do so on commercially reasonable terms, which would materially adversely affect our ability to bring products based on that technology to market. In addition, we depend on our licensors for assistance in developing products from licensed technology. If these licensors fail to perform or their performance is not satisfactory, our ability to successfully bring products to market may be delayed or impeded.~~

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We face intense competition and rapid technological changes and our failure to successfully compete or adapt to changing technology could make it difficult to successfully bring products to market.

The medical field is subject to rapid technological change and innovation. Pharmaceutical and biomedical research and product development are rapidly evolving fields in which developments are expected to continue at a rapid pace. Reports of progress and potential breakthroughs are occurring with increasing frequency. Our success will depend upon our ability to develop and maintain a competitive position in the research, development and commercialization of products and technologies in our areas of focus. Competition from pharmaceutical, chemical, biomedical and medical companies, universities, research and other institutions is intense and is expected to increase. All, or substantially all, of these competitors have substantially greater research and development capabilities, experience, and manufacturing, marketing, financial and managerial resources. Further, acquisitions of competing companies by large pharmaceutical or other companies could enhance such competitors' financial, marketing and other capabilities. Developments by others may render our products or technologies obsolete or not commercially viable and we may not be able to keep pace with technological developments.

We are subject to significant government regulation and failure to achieve regulatory approval for our products would severely harm our business.

Our ongoing research and development projects are subject to rigorous FDA approval procedures. The preclinical and clinical testing requirements to demonstrate safety and efficacy in each clinical indication (the specific condition intended to be treated) and regulatory approval processes of the FDA can take a number of years and will require us to expend substantial resources. We may be unable to obtain FDA approval for our products, and even if we do obtain approval, delays in such approval would adversely affect the marketing of products to which we have rights and our ability to receive product revenues or royalties. Moreover, even if FDA approval is obtained, a marketed product, its manufacturer and its manufacturing facilities are subject to continual review and periodic inspections by the FDA, and a later discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions on such product or manufacturer. Failure to comply with the applicable regulatory requirements can, among other things, result in fines, suspensions of regulatory approvals, product recalls, operating restrictions and criminal prosecution. Additional government regulation may be established which could prevent or delay regulatory approval of our products. Sales of pharmaceutical products outside the United States are subject to foreign regulatory requirements that vary widely from country to country. Even if FDA approval has been obtained, approval of a product by comparable regulatory authorities of foreign countries must be obtained prior to the commencement of marketing the product in those countries. The time required to obtain such approval may be longer or shorter than that required for FDA approval. We have no experience in manufacturing or marketing in foreign countries nor in matters such as currency regulations, import-export controls or other trade laws. To date, we have not received final regulatory approval from the FDA or any other comparable foreign regulatory authority for any of our products or technologies.

Our failure to meet product release schedules would make it difficult to predict

our quarterly results and may cause our operating results to vary significantly.

Delays in the planned release of our products may adversely affect forecasted revenues and create operational inefficiencies resulting from staffing levels designed to support the forecasted revenues. Our failure to introduce new products on a timely basis could delay or hinder market acceptance and allow competitors to gain greater market share.

If our intellectual property and proprietary rights are infringed, or infringe upon the rights of others, our business will suffer.

Our success will depend in part on our ability to obtain patent protection for our technologies, products and processes and to maintain trade secret protection and operate without infringing the proprietary rights of others. The degree of patent protection to be afforded to pharmaceutical, biomedical or medical inventions is an uncertain area of the law. In addition, the laws of foreign countries do not protect our proprietary rights to the same extent as do the laws of the United States. We may not develop or receive sublicenses or other rights related to proprietary technology that are patentable, patents that are pending may be not issued, and any issued patents may not provide us with any competitive advantages and may be challenged by third parties. Furthermore, others may independently duplicate or develop similar products or technologies to those developed by or licensed to us. If we are required to defend against charges of patent infringement or to protect our own proprietary rights against third parties, substantial costs will be incurred and we could lose rights to certain products and technologies or be required to enter into costly royalty or licensing agreements.

We do not have any marketing or manufacturing capabilities and will likely rely on third parties for these capabilities in order to bring products to market.

We do not currently have our own sales force or an agreement with another pharmaceutical company to market all of our products that are in development. When appropriate, we may build or otherwise acquire the necessary marketing capabilities to promote our products. However, we may not have the resources available to build or otherwise acquire our own marketing capabilities, and we may be unable to reach agreements with other pharmaceutical companies to market our products on terms acceptable to us, if at all.

In addition, we do not intend to manufacture our own products. While we have already entered into two manufacturing and supply agreements related to the MSI system and one related to the ADDS, these manufacturing and supply agreements may not be adequate and we may not be able to enter into future manufacturing and supply agreements on acceptable terms, if at all. Our reliance on independent manufacturers involves a number of risks, including the absence of adequate capacity, the unavailability of, or interruptions in, access to necessary manufacturing processes and reduced control over product quality and delivery schedules. If our manufacturers are unable or unwilling to continue manufacturing our products in required volumes, we will have to identify acceptable alternative manufacturers. The use of a new manufacturer may cause significant interruptions in supply if the new manufacturer has difficulty manufacturing products to our specifications. Further, the introduction of a new manufacturer may increase the variation in the quality of our products.

Healthcare reimbursement policies are uncertain and may adversely impact the sale of our products.

Our ability to commercialize human therapeutic and diagnostic products may depend in part on the extent to which costs for such products and technologies are reimbursed by private health insurance or government health programs. The uncertainty regarding reimbursement may be especially significant in the case of newly approved products. Reimbursement price levels may be insufficient to provide a return to us on our investment in new products and technologies. In the United States, government and other third-party payers have sought to contain healthcare costs by limiting both coverage and the level of reimbursement for new pharmaceutical products approved for marketing by the FDA, including some cases refusal to cover such approved products. Healthcare reform may increase these cost containment efforts. We believe that managed care organizations may seek to restrict the use of new products, delay authorization to use new products or limit coverage and the level of reimbursement for new products. Internationally, where national healthcare systems are prevalent, little if any funding may be available for new products, and cost containment and cost reduction efforts can be more pronounced than in the United States.

We may become subject to product liability claims and our product liability insurance may be inadequate.

The use of our proposed products and processes during testing, and after approval, may entail inherent risks of adverse effects that could expose us to product liability claims and associated adverse publicity. Although we currently maintain general liability insurance, the coverage limits of our insurance policies may not be adequate. We currently maintain clinical trial product liability insurance of $2.0 million per event for certain clinical trials and intend to obtain insurance for future clinical trials of products under development. However, we may be unable to obtain or maintain insurance for any future clinical trials. Such insurance is expensive, difficult to obtain and may not be available in the future on acceptable terms, or at all. A successful claim brought against us in excess of our insurance coverage would have a material adverse effect upon us and our financial condition. We intend to require our licensees to obtain adequate product liability insurance. However, licensees may be unable to maintain or obtain adequate product liability insurance on acceptable terms and such insurance may not provide adequate coverage against all potential claims.

If our common stock is delisted from the American Stock Exchange, the price of our common stock and its liquidity could decline.

Our common stock is listed for trading on the American Stock Exchange, or AMEX, under the symbol "SHM". We do not satisfy discretionary AMEX guidelines for continued listing, including a guideline that a listed company that has sustained losses from operations and/or net losses in three of its four most recent fiscal years, have stockholders' equity of at least $4,000,000. We had net capital deficiency of $413,720 at December 31, 2000. We also do not satisfy a guideline against continued losses for each of the issuer's five most recent fiscal years. Our continued failure to meet the listing guidelines has been regularly reviewed by AMEX and may ultimately result in our common stock being delisted from AMEX. If our common stock were delisted from AMEX, trading of our

common stock, if any, would thereafter likely be conducted in the over-the-counter market, unless we were able to list our common stock on The Nasdaq Stock Market or another national securities exchange, which cannot be assured. If our common stock were to trade in the over-the-counter market it may be more difficult for investors to dispose of, or to obtain accurate quotations as to the market value of our common stock. In addition, it may become more difficult for us to raise funds through the sale of our securities.

In the event of the delisting of our common stock from the AMEX and our inability to list our common stock on The Nasdaq Stock Market or another national securities exchange, the regulations of the SEC under the Securities Exchange Act of 1934, as amended, require additional disclosure relating to the market for penny stocks. SEC regulations generally define a penny stock to be an equity security that has a market price of less than $5.00 per share, subject to certain exceptions. A disclosure schedule explaining the penny stock market and the risks associated therewith is required to be delivered to a purchaser and various sales practice requirements are imposed on broker-dealers who sell penny stocks to persons other than established customers and accredited investors (generally institutions). In addition, the broker-dealer must provide the customer with current bid and offer quotations for the penny stock, the compensation of the broker-dealer and its salesperson in the transaction and monthly account statements showing the market value of each penny stock held in the customer's account. If our securities become subject to the regulations applicable to penny stocks, the market liquidity for our securities could be severely affected. In such an event, the regulations on penny stocks could limit the ability of broker-dealers to sell our securities.

The price of biotechnology/pharmaceutical company stocks has been volatile which could result in substantial losses to our stockholders.

The market price of securities of companies in the biotechnology/pharmaceutical industries has tended to be volatile. Announcements of technological innovations by us or our competitors, developments concerning proprietary rights and concerns about safety and other factors may have a material effect on our business or financial condition. The market price of our common stock may be significantly affected by announcements of developments in the medical field generally or our research areas specifically. The stock market has experienced volatility in market prices of companies similar to us that has been unrelated to the operating results of such companies. This volatility may have a material adverse effect on the market price of our common stock.

Our ability to issue "blank check" preferred stock may make it more difficult for a change in our control.

Our certificate of incorporation authorizes the issuance of "blank check" preferred stock with such designations, rights and preferences as may be determined from time to time by the Board of Directors, without shareholder approval. In the event of issuance, such preferred stock could be utilized, under certain circumstances, as a method of discouraging, delaying or preventing a change in our control and preventing shareholders from receiving a premium for their shares in connection with a change of control. We issued Series A and Series B cumulative convertible redeemable preferred stock in connection with private placements in February 1997 and April 1998, respectively. All of the

Series A preferred stock was converted into common stock during 1998. On July 31, 1998, all of the Series B Preferred stock was redeemed for cash. We also issued shares of our Series C cumulative convertible preferred stock in connection with the consummation of an agreement with Elan International Services, Ltd. ("Elan International") in June 1998. In October 1999, in conjunction with a licensing agreement with Elan International, we issued shares of our Series D cumulative convertible exchangeable preferred stock and Series F cumulative convertible preferred stock. In addition, we also have a commitment from Elan International to purchase shares of Series E cumulative convertible non-exchangeable preferred stock at our option (subject to satisfaction of certain conditions). Except for the previously-mentioned purchase commitment for Series E preferred stock, and additional shares of Series C, D and E preferred stock that may be payable as dividends to Elan International, as holder of the outstanding Series C, D and E preferred stock, we have no present intention to issue any additional shares of our preferred stock; however, we may issue additional shares of our preferred stock in the future.

We have granted anti-dilutions rights to The Tail Wind Fund Ltd. which may require us to issue additional shares to Tail Wind, make cash payments to Tail Wind and may hinder our ability to raise additional funds.

Pursuant to our December 2000 private placement with The Tail Wind Fund Ltd., until at least August 29, 2002, if we sell shares of our common stock or securities convertible into or exercisable for common stock for less than $3.5888 per share, we are obligated to issue to Tail Wind additional shares so that the number of shares purchased by Tail Wind in the December 2000 private placement plus the additional shares issued to Tail Wind equals the number of shares that Tail Wind could have purchased for $2,250,000 at the price per share at which the new shares are sold. The presence of these anti-dilution rights may negatively affect our ability to obtain additional financing. In addition, in the event that we are required to issue additional shares to Tail Wind, we may not issue an aggregate of over 5,630,122 shares of our common stock in total to Tail Wind in connection with the December 2000 private placement. If we would otherwise be required to issue more than 5,630,122 shares to Tail Wind, we must instead pay Tail Wind 105% of the cash value of such shares we do not issue.

We are obligated to issue additional securities in the future diluting our stockholders.

As of December 31, 2000, we had reserved approximately 6,921,629 shares of our common stock for issuance upon exercise of outstanding options and warrants convertible into shares of our common stock, including by our officers and directors. In addition, as of December 31, 2000, we had $2,000,000 principal amount of a convertible promissory note, 13,712 shares of our Series C preferred stock, 12,870 shares of our Series D preferred stock, 1,004 shares of our Series E preferred stock and 5,000 shares of our Series F preferred stock outstanding. Each of the convertible securities provides for conversion into shares of our common stock at a discount to the market price at December 31, 2000. Our Series C, D, E and F preferred stock are convertible into 9,724,823 shares, 2,648,148 shares, 258,098 shares and 1,470,588 shares, respectively, of common stock. The convertible promissory note, including accrued interest is convertible into 1,362,578 shares of common stock. The exercise of options and outstanding warrants, the conversion of such other securities and sales of common stock

issuable thereunder could have a significant dilutive effect on the market price of our common stock and could materially impair our ability to raise capital through the future sale of our equity securities.

ITEM 2. PROPERTIES

The Company's principal executive offices are located at 425 South Woodsmill Road, St. Louis, Missouri 63017. These premises consist of approximately 4,521 square feet subject to a lease that expires September 14, 2002. The monthly rent for these premises is $9,419. The Company also maintains a research facility in Ann Arbor, Michigan, and leases a small office in Rochester, New York. The Company maintains no other laboratory, research or other facilities, but primarily conducts research and development in outside laboratories under contracts with universities or research facilities. The Company believes that its existing office arrangements will be adequate to meet its reasonably foreseeable future needs.

ITEM 3. LEGAL PROCEEDINGS

There are no material legal proceedings against the Company or any of its subsidiaries.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

None.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS

The following table sets forth the high and low sale prices of the Company's Common Stock on the American Stock Exchange (the "AMEX") for the periods indicated.

2000:	High	Low
Fourth Quarter	$6.625	$3.250
Third Quarter	6.875	4.250
Second Quarter	5.938	3.000
First Quarter	7.938	3.375

1999:	High	Low
Fourth Quarter	$5.250	$2.438
Third Quarter	2.938	2.000
Second Quarter	3.063	2.188
First Quarter	3.500	2.000

The closing sale price for the Company's Common Stock on the AMEX on March 6, 2001 was $3.70 per share. At March 6, 2001, there were approximately 413 holders of record of the Company's Common Stock.

The Company has never paid dividends on its Common Stock and does not intend to pay cash dividends on its Common Stock in the foreseeable future. The terms of the Company's Series C, D and E Preferred Stock generally prohibit the payment of cash dividends and other distributions on the Company's Common Stock unless full cumulative stock dividends on shares of such Series C, D and E Preferred Stock have been paid or declared in full. During 2000, the Company issued stock dividends totaling 932, 855 and 4 shares and cash dividends for fractional shares of $2,045, $750, and $750 on Series C, D and E Preferred Stock, respectively.

The following unregistered securities were issued by the Company during the quarter ended December 31, 2000:

DATE OF SALE/ISSUANCE	DESCRIPTION OF SECURITIES ISSUED	NUMBER OF SHARES SOLD/ISSUED/ SUBJECT TO OPTIONS OR WARRANTS	OFFERING/ EXERCISE PRICE PER SHARE ($)	PURCHASER OR CLASS
	Warrant to purchase shares of			
October 2, 2000	Common Stock, $.01 par value	35,000	$6.125	Accredited Investor
December 29, 2000	Common Stock, $.01 par value	626,950	$3.5888	Accredited Investor
	Warrant to purchase shares of			
December 29, 2000	Common Stock, $.01 par value	18,808	$4.9844	Accredited Investor
	Warrant to purchase shares of			
December 29, 2000	Common Stock, $.01 par value	18,808	$4.9844	Accredited Investor
	Warrant to purchase shares of			
December 29, 2000	Common Stock, $.01 par value	112,500	$4.9844	Accredited Investor

The issuance of these securities are claimed to be exempt from registration pursuant to Section 4(2) of the Securities Act of 1933, as amended, as transactions by an issuer not involving a public offering. There were no underwriting discounts or commissions paid in connection with the issuance of any of these securities.

ITEM 6. SELECTED FINANCIAL DATA

The information required by this Item is incorporated by reference to the Company's Annual Report to Stockholders for the year ended December 31, 2000, pertinent portions of which are attached hereto as Exhibit 13.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OR PLAN OF OPERATION

The information required by this Item is incorporated by reference to the Company's Annual Report to Stockholders for the year ended December 31, 2000, pertinent portions of which are attached hereto as Exhibit 13.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISK

The Company has no material market risk exposure.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Quarterly financial data for 2000 and 1999 is summarized below:

	Three Months Ended			
	Mar 31	Jun 30	Sep 30	Dec 31
2000:				
Total revenues	$ 121,170	$ 124,505	$ 46,109	$ 214,788
Operating loss	(1,475,577)	(1,449,671)	(1,367,362)	(1,765,790)
Net loss	(1,457,090)	(1,383,810)	(1,318,141)	(1,604,110)
Basic and diluted net loss per share	(.05)	(.05)	(.05)	(.06)
1999:				
Total revenues	$ 26,000	$ 101,412	$ 147,526	$ 124,440
Operating loss	(1,154,642)	(1,468,668)	(1,418,452)	(16,257,730)
Net loss	(1,162,656)	(1,487,010)	(1,454,942)	(13,280,180)
Basic and diluted net loss per share	(.04)	(.05)	(.05)	(.49)

The remaining information required by this Item is incorporated by reference to the Company's Annual Report to Stockholders for the year ended December 31, 2000, pertinent portions of which are attached hereto as Exhibit 13.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS, PROMOTERS AND CONTROL PERSONS; COMPLIANCE WITH SECTION 16(A) OF THE EXCHANGE ACT

The information required by this Item is incorporated by reference to the Company's definitive proxy statement to be filed no later than April 30, 2001, pursuant to Regulation 14A of the General Rules and Regulations under the Securities Exchange Act of 1934.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item is incorporated by reference to the Company's definitive proxy statement to be filed no later than April 30, 2001, pursuant to Regulation 14A of the General Rules and Regulations under the Securities Exchange Act of 1934.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The information required by this Item is incorporated by reference to the Company's definitive proxy statement to be filed no later than April 30, 2001, pursuant to Regulation 14A of the General Rules and Regulations under the Securities Exchange Act of 1934.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

The information required by this Item is incorporated by reference to the Company's definitive proxy statement to be filed no later than April 30, 2001, pursuant to Regulation 14A of the General Rules and Regulations under the Securities Exchange Act of 1934.

ITEM 14. EXHIBITS, FINANCIAL STATEMENT SCHEDULES AND REPORTS ON FORM 8-K

(a)(1) Financial Statements

The following Financial Statements are included in Exhibits 13 hereto:
Report of Independent Auditors
Consolidated Balance Sheets as of December 31, 2000 and 1999
Consolidated Statements of Operations for the years ended December 31, 2000, 1999 and 1998 and for the period October 17, 1986 (inception) to December, 31 2000
Consolidated Statements of Stockholders' Equity (net capital deficiency) for the period from October 17, 1986 (inception) to December 31, 2000
Consolidated Statements of Cash Flows for the years ended December 31, 2000, 1999 and 1998 and for the period from October 17, 1986 (inception) to December 31, 2000
Notes to Financial Statements

(a)(2) Financial Statement Schedules

All financial statement schedules are omitted because they are not applicable, or not required, or because the required information is included in the financial statements or notes thereto.

(a)(3) Exhibits:

NO.		REFERENCE
3.1	Certificate of Incorporation of the Company, as amended	(10)
3.2	By-Laws of the Company	(4)
4.1	Form of Common Stock Certificate	(2)
4.4	Certificate of Designations defining the powers, designations, rights, preferences, limitations and restrictions applicable to the Company's Series C Cumulative Convertible Redeemable Preferred Stock.	(10)

NO.		REFERENCE
4.5	Certificate of Designations defining the powers, designations, rights, preferences, limitations and restrictions applicable to the Company's Series D Cumulative Convertible Exchangeable Preferred Stock.	(15)
4.6	Certificate of Designations defining the powers, designations, rights, preferences, limitations and restrictions applicable to the Company's Series E Convertible Non-Exchangeable Preferred Stock.	(15)
4.7	Certificate of Designations defining the powers, designations, rights, preferences, limitations and restrictions applicable to the Company's Series F Convertible Non-Exchangeable Preferred Stock.	(15)
10.6	Employment Agreement dated as of June 6, 1996 between the Company and Thomas M. Fitzgerald*	(3)
10.6.5	Employment Agreement dated as of November 16, 1998 between the Company and Scott Hoffmann*	(14)
10.8	1993 Stock Option Plan, as amended*	(1)
10.9	1993 Restricted Stock Plan, as amended*	(1)
10.10	1996 Directors Stock Option Plan*	(7)
10.11	Agreement and Plan of Merger among the Company, Camelot Pharmacal, L.L.C., David A. Byron, Loren G. Peterson and Carl Siekmann dated April 25, 1997*	(6)
10.12	Employment Agreement dated as of April 25, 1997 between the Company and David A. Byron*	(6)
10.13	Employment Agreement dated as of April 25, 1997 between the Company and Loren G. Peterson*	(6)
10.14	Employment Agreement dated as of April 25, 1997 between the Company and Carl Siekmann*	(6)
10.15	Form of the Company's 6% Convertible Subordinated Debentures due September 22, 2000.	(8)
10.16	Lease dated August 18, 1997 between Corporate Center, L.L.C. and the Company relating to the lease of office space in St. Louis, Missouri.	(5)
10.17	Assignment and License Agreement dated as of December 3, 1997 between 1266417 Ontario Limited and Ion Pharmaceuticals, Inc. (portions of this exhibit were omitted and were filed separately with the Securities Exchange Commission pursuant to the Company's application requesting confidential treatment in accordance with Rule 24b-2 as promulgated under the Securities	(9)

Exchange Act of 1934, as amended).

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NO.		REFERENCE
10.18	Sub-License Agreement dated as of December 3, 1997 between 1266417 Ontario Limited and Ion Pharmaceuticals, Inc. (portions of this exhibit were omitted and were filed separately with the Securities Exchange Commission pursuant to the Company's application requesting confidential treatment in accordance with Rule 24b-2 as promulgated under the Securities Exchange Act of 1934, as amended).	(9)
10.19	Form of Sublicense and Development Agreement between Sheffield Pharmaceuticals, Inc. and Inpharzam International, S.A. (portions of this exhibit were omitted and were filed separately with the Securities and Exchange Commission pursuant to the Company's application requesting confidential treatment in accordance with Rule 24b-2 as promulgated under the Securities Exchange Act of 1934, as amended).	(12)
10.20	Securities Purchase Agreement, dated as of June 30, 1998, by and between Sheffield pharmaceuticals, Inc. and Elan International Services, Ltd., which includes the Certificate of Designations of Series C Convertible Preferred Stock as Exhibit B. The Company agreed to furnish the disclosure schedules as well as Exhibits A and C, which were omitted from this filing, to the Commission upon request (portions of this exhibit were omitted and were filed separately with the Securities and Exchange Commission pursuant to the Company's application requesting confidential treatment in accordance with Rule 24b-2 as promulgated under the Securities Exchange Act of 1934, as amended).	(13)
10.21	Systemic Pulmonary Delivery, Ltd. Joint Development and Operating Agreement dated as of June 30, 1998 among Systemic Pulmonary Delivery, Ltd., Sheffield Pharmaceuticals, Inc. and Elan International Services, Ltd. (portions of this exhibit were omitted and were filed separately with the Securities and Exchange Commission pursuant to the Company's application requesting confidential treatment in accordance with Rule 24b-2 as promulgated under the Securities Exchange Act of 1934, as amended).	(13)
10.22	License and Development Agreement dated June 30, 1998 between Sheffield Pharmaceuticals, Inc. and Systemic Pulmonary Delivery, Ltd. and Elan Corporation plc. (portions of this exhibit were omitted and were filed separately with the Securities and Exchange Commission pursuant to the Company's application requesting confidential treatment in accordance with Rule 24b-2 as promulgated under the Securities Exchange Act of 1934, as amended).	(13)

NO.		REFERENCE
10.23	License and Development Agreement dated June 30, 1998 between Systemic Pulmonary Delivery, Ltd. and Sheffield Pharmaceuticals, Inc. and Elan Corporation, plc. (portions of this exhibit were omitted and were filed separately with the Securities and Exchange Commission pursuant to the Company's application requesting Rule 24b-2 as promulgated under the Securities Exchange Act of 1934, as amended).	(13)
10.24	License and Development Agreement dated June 30, 1998 between Elan Corporation, plc and Systemic Pulmonary Delivery, Ltd. and Sheffield Pharmaceuticals, Inc. (portions of this exhibit were omitted and were filed separately with the Securities and Exchange Commission pursuant to the Company's application requesting confidential treatment in accordance with Rule 24b-2 as promulgated under the Securities Exchange Act of 1934, as amended).	(13)
10.25	Securities Purchase Agreement, dated as of October 18, 1999, by and between the Company and Elan (portions of this exhibit were omitted and were filed separately with the Securities and Exchange Commission pursuant to the Company's application requesting confidential treatment in accordance with Rule 24b-2 as promulgated under the Securities Exchange Act of 1934, as amended).	(15)
10.26	Subscription, Joint Development and Operating Agreement dated as of October 18, 1999 by and among Elan Pharma International Limited, Elan, the Company and Newco. (portions of this exhibit were omitted and were filed separately with the Securities and Exchange Commission pursuant to the Company's application requesting confidential treatment in accordance with Rule 24b-2 as promulgated under the Securities Exchange Act of 1934, as amended).	(15)
010.27	License Agreement, dated as of October 19, 1999, by and between the Company and Newco (portions of this exhibit were omitted and were filed separately with the Securities and Exchange Commission pursuant to the Company's application requesting confidential treatment in accordance with Rule 24b-2 as promulgated under the Securities Exchange Act of 1934, as amended).	(15)
10.28	License Agreement, dated as of October 19, 1999, by and between Elan Pharma International Limited and Newco (portions of this exhibit were omitted and were filed separately with the Securities and Exchange Commission pursuant to the Company's application requesting confidential treatment in accordance with Rule 24b-2 as promulgated under the Securities	(15)

Exchange Act of 1934, as amended).

10.29	Registration Rights Agreement dated as of October 18, 1999 by and between Elan and the Company.	(15)

NO.	REFERENCE
10.30	Securities Purchase Agreement dated as of December 29, 2000, by and between the Company and The Tail Wind Fund Ltd	(16)
10.31	Registration Rights Agreement dated as of December 29, 2000, by and between the Company and The Tail Wind Fund Ltd	(16)
13	Portions of the Company's Annual Report to Stockholders for the year ended December 31, 2000 relating to Items 6, 7 and 8.	(1)
21	Subsidiaries of Registrant	(1)
23.1	Consent of Ernst & Young LLP	(1)
24	Power of Attorney (Included on page 29 hereof)	(1)

* Management contracts or compensatory plans or arrangements.

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(1) Filed herewith.
(2) Incorporated by reference to the Company's Annual Report on Form 10-KSB for its fiscal year ended December 31, 1995 filed with the Securities and Exchange Commission.
(3) Incorporated by reference to the Company's Quarterly Report on Form 10-QSB for the quarter ended June 30, 1996 filed with the Securities and Exchange Commission.
(4) Incorporated by reference to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 1997 filed with the Securities and Exchange Commission.
(5) Incorporated by reference to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 1997 filed with the Securities and Exchange Commission.
(6) Incorporated by reference to the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 1997 filed with the Securities and Exchange Commission.
(7) Incorporated by reference to the Company's Annual Report on Form 10-KSB for the year ended December 31, 1996 filed with the Securities and Exchange Commission.
(8) Incorporated by reference to the Company's Registration Statement on

Form S-3 (File No. 333-38327) filed with the Securities and Exchange Commission on October 21, 1997.

(9) Incorporated by reference to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on December 17, 1997.

(10) Incorporated by reference to the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 1998 filed with the Securities and Exchange Commission.

(11) Incorporated by reference to Exhibit 3 of the Company's Current Report on Form 8-K, dated April 17, 1998, filed with the Securities and Exchange Commission.

(12) Incorporated by reference to Exhibit 2 of the Company's Current Report on Form 8-K, dated June 22, 1998, filed with the Securities and Exchange Commission.

(13) Incorporated by reference to exhibits to the Company's Current Report on Form 8-K, dated July 16, 1998, filed with the Securities and Exchange Commission.

(14) Incorporated by reference to the Company's Annual Report on Form 10-K for the year ended December 31, 1998 filed with the Securities and Exchange Commission.

(15) Incorporated by reference to the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on November 2, 1999.

(16) Incorporated by reference to the Company's Registration Statement on Form S-3 (File No. 333-54446) filed with the Securities and Exchange Commission on January 26, 2001.

(b) Reports on Form 8-K

(1) Current Report on Form 8-K filed with Securities and Exchange Commission on November 14, 2000.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

SHEFFIELD PHARMACEUTICALS, INC.

Dated: March 9, 2001 /S/

Loren G. Peterson
President and Chief Executive Officer

POWER OF ATTORNEY

Sheffield Pharmaceuticals, Inc. and each of the undersigned do hereby appoint Loren G. Peterson and Thomas Fitzgerald and each of them severally, its or his or her true and lawful attorney to execute on behalf of Sheffield Pharmaceuticals, Inc. and the undersigned any and all amendments to this Annual Report and to file the same with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission; each of such attorneys shall have the power to act hereunder with or without the other.

In accordance with the Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
/S/ Thomas M. Fitzgerald	Chairman and Director	March 9, 2001
/S/ Loren G. Peterson	Director, President and Chief Executive Officer	March 9, 2001
/S/ John M. Bailey	Director	March 9, 2001
/S/ Digby W. Barrios	Director	March 9, 2001
/S/ Todd C. Davis	Director	March 9, 2001
/S/ Scott A. Hoffmann	Vice President, Chief Financial Officer, Treasurer and Secretary (Chief Financial and Chief Accounting Officer)	March 9, 2001